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OM protein - protein search, using sw model

Run on: November 8, 2004, 18:14:16; Search time 155 Seconds

(without alignments)

733.659 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

Sequence: 1 MRRASRDYTKYLRGSEEMGG.....LLDPDQDATYFGAFKVRDID 317

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 2002273 seqs, 358729299 residues

Total number of hits satisfying chosen parameters: 2002273

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database: A Geneseq 23Sep04:\*

1: geneseqp1980s:\*

2: geneseqp1990s:\*

3: geneseqp2000s:\*

4: geneseqp2001s:\*

5: geneseqp2002s:\*

6: geneseqp2003as:\*

7: geneseqp2003bs:\*

8: geneseqp2004s:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

			8					
R	esult		Query					
	No.	Score	Match	Length	DB	ID	Description	
		1685	100 0	217	 2	AAW83195	Aaw83195 Human os	·
	1	TOBS	100.0	317	2	AAWOJIJJ	<del></del>	
	2	1685	100.0	317	2	AAW69957	Aaw69957 NF-kB re	€C
	3	1685	100.0	317	2	AAW68293	Aaw68293 NF-kB re	ЭC
	4	1685	100.0	317	2	AAE08738	Aae08738 Human re	<b>∋</b> C
	5	1685	100.0	317	3	AAY84417	Aay84417 Amino ac	ci
	6	1685	100.0	317	4	AAE04426	Aae04426 Human re	3C
	7	1685	100.0	317	4	AAE01993	Aae01993 Human fu	ıl
	8	1685	100.0	317	5	ABB08134	Abb08134 Human RA	УN
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1.0	1.005	100 0	217	_	22221621	71 - 21 (21	
10	1685	100.0	317	5	ABG31631		Human RAN
11	1685	100.0	317	5	AAU78285		Human TRA
12	1685	100.0	317	5	AA019096		C neoform
13	1685	100.0	317	6	ABP55108	-	Human ost
14	1685	100.0	317	6	AAE34364		Human rec
15	1685	100.0	317	6	ABR42314	Abr42314	Human RAN
16	1685	100.0	317	7	ADB16988	Adb16988	Human rec
17	1685	100.0	317	7	ADC35204	Adc35204	Human TNF
18	1685	100.0	317	7	ADC73002	Adc73002	Human RAN
19	1685	100.0	317	7	ADC78268	Adc78268	Human RAN
20	1685	100.0	317	7	ABW02277	Abw02277	Human RAN
21	1685	100.0	317	7	ADG46723	Adg46723	Human RAN
22	1685	100.0	317	7	ADJ82112	Adj82112	Protein f
23	1685	100.0	317	8	ADM96241	Adm96241	Human rec
24	1677	99.5	317	2	AAW83018	Aaw83018	Osteoclas
25	1422	84.4	270	7	ADJ82113	Adj82113	Protein f
26	1417.5	84.1	316	2	AAW83017	Aaw83017	Osteoclas
27	1417.5	84.1	316	2	AAW83194	Aaw83194	Human ost
28	1417.5	84.1	316	2 -	AAW59654	Aaw59654	Amino aci
29	1417.5	84.1	316	2	AAY17874	Aay17874	Murine TR
30	1417.5	84.1	316	3	AAY91024		Mouse OBM
31	1417.5	84.1	316	3	AAY84418	Aay84418	Amino aci
32	1417.5	84.1	316	3	AAY84419	Aay84419	Amino aci
33	1417.5	84.1	316	5	AAU78289		Mouse TRA
34	1417.5	84.1	316	6	ABR42071	Abr42071	Human RAN
35	1417.5	84.1	316	6	ABB99477	Abb99477	Amino aci
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38	1396.5	82.9	318	4	AAB82092	Aab82092	Rat osteo
39	1326.5	78.7	294	2	AAW69956	Aaw69956	NF-kB rec
40	1326.5	78.7	294	2	AAW68292		NF-kB rec
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42	1326.5	78.7	294	4	AAE04425	Aae04425	Murine re
43	1326.5	78.7	294	4	AAE01992	Aae01992	Murine RA
44	1326.5	78.7	294	5	AAE26102		Mouse RAN
45	1326.5	78.7	294	7	ADB16986		Murine re

### ALIGNMENTS

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RESULT 1
AAW83195
     AAW83195 standard; protein; 317 AA.
XX
AC
    AAW83195;
XX
     11-FEB-1999 (first entry)
DT
XX
     Human osteoprotegerin binding protein from the pcDNA/huOPGbp1.linsert.
DE
XX
KW
     Human; osteoprotegerin binding protein; OPG binding protein; arthritis;
     osteoporosis; osteoclast maturation; bone disease; metastasis; ODAR;
KW
     hypercalcaemia; osteoclast differentiation and activation receptor;
KW
KW
     Paget's disease.
XX
os
     Homo sapiens.
```

```
XX
PN
    WO9846751-A1.
XX
PD
    22-OCT-1998.
XX
PF
    15-APR-1998;
                   98WO-US007584.
XX
                   97US-00842842.
PR
    16-APR-1997;
    23-JUN-1997;
                   97US-00880855.
PR
PR
    30-MAR-1998;
                   98US-00052521.
XX
PA
     (AMGE-) AMGEN INC.
XX
PΙ
    Boyle WJ;
XX
    WPI; 1998-594578/50.
DR
    N-PSDB; AAV70285.
DR
XX
PТ
    Nucleic acid encoding osteoprotegrin binding protein - useful for, e.g.
PT
    treating bone diseases by modulating osteoclast differentiation and for
PT
    diagnosis.
XX
    Claim 19; Fig 4; 47pp; English.
PS
XX
    The present sequence is human osteoprotegerin (OPG) binding protein. Host
CC
CC
    cells transfected with vectors containing nucleic acid molecules encoding
CC
    OPG binding protein are used to produce recombinant OPG binding protein.
CC
    OPG binding protein is used in binding assays to determine osteoprotegrin
CC
     (OG) in biological samples; to screen for specific binding agents
CC
     (particularly agonists and antagonists, including intracellular proteins)
CC
     ; to raise Ab (useful in immunoassays for detection of OPG binding
СC
    protein) and to identify compounds that modulate binding of OPG binding
CC
    protein to osteoclast differentiation and activation receptor (ODAR). The
CC
    nucleic acid molecule encoding OPG binding protein can be used to detect
CC
    OPG binding protein-encoding sequences, e.g. screening for related
CC
    sequences, also to produce transgenic animal models, while complementary
CC
    sequences are used for antisense regulation of OPG binding protein
CC
    expression. Modulators of OPG binding protein, particularly soluble forms
CC
    of OPG binding protein or Ab, are used to treat or prevent bone diseases,
CC
    e.g. osteoporosis, bone loss caused by arthritis or metastases,
CC
    hypercalcaemia, Paget's disease, periodontal disease, osteoporosis,
CC
    loosening of prostheses, optionally in combination with agents that
CC
    promote bone growth
XX
SO
    Sequence 317 AA;
  Query Match
                         100.0%;
                                 Score 1685; DB 2;
                         100.0%;
  Best Local Similarity
                                 Pred. No. 6.2e-154;
 Matches 317; Conservative
                               0; Mismatches
                                                 0; Indels
                                                              0;
                                                                  Gaps
                                                                          0;
Qу
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Qу
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Db
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Qy
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Qу
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Db
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Qy
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
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         301 PDQDATYFGAFKVRDID 317
Qу
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         301 PDQDATYFGAFKVRDID 317
Db
RESULT 2
AAW69957
    AAW69957 standard; protein; 317 AA.
XX
AC
    AAW69957;
XX
    08-OCT-1998 (first entry)
DΤ
XX
DE
    NF-kB receptor activator RANK ligand (RANKL).
XX
KW
    RANK; necrosis factor-kappa B; NF-kB; receptor activator; human;
KW
    immune response; inflammatory response; toxic shock; sepsis; RANKL;
KW
    RANK ligand; tumour necrosis factor; TNF.
XX
OS
    Homo sapiens.
XX
PN
    WO9828426-A2.
XX
PD
    02-JUL-1998.
XX
PF
    22-DEC-1997;
                  97WO-US023775.
XX
PR
    23-DEC-1996;
                  96US-0059978P.
                  97US-00813509.
PR
    07-MAR-1997;
PR
    14-OCT-1997;
                  97US-0064671P.
XX
PA
    (IMMV ) IMMUNEX CORP.
XX
PΙ
    Anderson DM, Galibert LJ, Maraskovsky E;
XX
DR
    WPI; 1998-377657/32.
DR
    N-PSDB; AAV41378.
XX
PT
    New isolated ligand for receptor activator of NF-kappa B - used to
PT
    develop products for augmenting an immune response for inhibiting an
    inflammatory response and for protection of cells.
PT
XX
PS
    Claim 27; Page 59-60; 80pp; English.
XX
```

```
CC
     This represents a human RANKL, a ligand for the RANK (receptor activator
CC
     of necrosis factor-kappaB (NF-kB)) polypeptide. RANK is a member of the
CC
     tumour necrosis factor (TNF) family. A soluble RANK may be used for
CC
     inhibiting activation of NF-kB, by contacting a cell expressing membrane-
CC
     associated RANK with a soluble RANK which binds to RANK ligand (RANKL).
     RANKL polypeptides can activate RANK and can be used to induce maturation
CC
CC
     of dendritic cells and enhance their allo-stimulatory capacity, thereby
CC
     augmenting an immune response. The soluble RANK polypeptide composition
CC
     may also be used for regulating an immune or inflammatory response.
CC
     Inhibition of NF-kB by RANK antagonists may be useful in ameliorating
CC
     negative effects of an inflammatory response that result from triggering
     of RANK, e.q. in treating toxic shock or sepsis, graft-versus-host
CC
     reactions, or acute inflammatory reactions. They can also be used in
CC
CC
     adjunct therapy for disease characterised by neoplastic cells that
     express RANK. RANKL polypeptides can also be used to identify inhibitors
CC
     of RANK and thus inhibitors of an inflammatory response, and also for
CC
CC
     protecting RANK-expressing cells from the negative effects of
CC
     chemotherapy or the presence of high levels of TNF-alpha. The products
     can also be used for detection and drug screening
CC
XX
```

SQ Sequence 317 AA;

```
100.0%;
                          Score 1685; DB 2; Length 317;
 Query Match
 Best Local Similarity
                   100.0%; Pred. No. 6.2e-154;
 Matches 317; Conservative
                         0; Mismatches
                                         Indels
                                                    Gaps
                                                          0;
                                      0;
                                                 0;
         1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
          Db
         1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
        61 VCSVALFFYFRAOMDPNRISEDGTHCIYRILRLHENADFODTTLESODTKLIPDSCRRIK 120
Qу
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
Qу
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          121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
Qy
       181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
          181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
       241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qy
          241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
Qy
       301 PDQDATYFGAFKVRDID 317
          1111111111
       301 PDQDATYFGAFKVRDID 317
Db
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#### RESULT 3 AAW68293

ID AAW68293 standard; protein; 317 AA.

XX

AC AAW68293;

XX

```
08-OCT-1998 (first entry)
DT
XX
     NF-kB receptor activator RANK ligand (RANKL).
DE
ХX
KW
     RANK; necrosis factor-kappa B; NF-kB; receptor activator; human;
KW
     immune response; inflammatory response; toxic shock; sepsis; RANKL;
     RANK ligand; tumour necrosis factor; TNF.
KW
XX
OS
     Homo sapiens.
XX
PN
     WO9828424-A2.
XX
     02-JUL-1998.
PD
XX
PF
     22-DEC-1997;
                    97WO-US023866.
XX
                    96US-0059978P.
PR
     23-DEC-1996;
     07-MAR-1997;
                    97US-00813509.
PR
     14-OCT-1997;
                    97US-0064671P.
PR
XX
     (IMMV ) IMMUNEX CORP.
PA
XX
PΙ
     Anderson DM, Galibert LJ, Maraskovsky E;
XX
     WPI; 1998-377655/32.
DR
     N-PSDB; AAV41372.
DR
XX
PT
     New isolated receptor activator of necrosis factor-kappa B - useful for,
     e.g. developing products for regulating an immune or inflammatory
PT
PT
     response, treating toxic shock or sepsis.
XX
PS
     Example 7; Page 59-60; 80pp; English.
XX
CC
     This represents a human RANKL, a ligand for the RANK (receptor activator
CC
     of necrosis factor-kappaB (NF-kB)) polypeptide. RANK is a member of the
CC
     tumour necrosis factor (TNF) family. Host cells transformed or
     transfected with an expression vector comprising the RANK encoding
CC
     nucleic acid can be used to produce recombinant RANK protein. The soluble
CC
CC
     RANK may be used for inhibiting activation of NF-kB, by contacting a cell
     expressing membrane-associated RANK with a soluble RANK which binds to
CC
     RANK liqand (RANKL). The soluble RANK polypeptide composition may also be
CC
     used for regulating an immune or inflammatory response. Inhibition of NF-
CC
CC
     kB by RANK antagonists may be useful in ameliorating negative effects of
     an inflammatory response that result from triggering of RANK, e.g. in
CC
     treating toxic shock or sepsis, graft-versus-host reactions, or acute
CC
     inflammatory reactions. They can also be used in adjunct therapy for
CC
CC
     disease characterised by neoplastic cells that express RANK. The products
     can also be used for detection and drug screening
CC
XX
SO
     Sequence 317 AA;
  Query Match
                          100.0%; Score 1685; DB 2; Length 317;
                          100.0%; Pred. No. 6.2e-154;
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  Matches 317; Conservative
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                                                   0; Indels
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Qу
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Db
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Qу
            1111111111111111
        301 PDQDATYFGAFKVRDID 317
Db
RESULT 4
AAE08738
ID
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XX
AC
    AAE08738;
XX
DT
    15-NOV-2001 (first entry)
XX
DE
    Human receptor activator of NF kappaB ligand (RANKL) protein.
XX
KW
    Human; receptor activator of nuclear factor kappaB ligand; RANKL; NF;
    tumour necrosis factor; TNF; TNF receptor associated factor; TRAF;
KW
    immune response; inflammatory response; graft-versus-host reaction;
KW
    toxic shock; sepsis; acute inflammatory reaction; bone resorption;
KW
    anti-apoptotic signal; therapy; immunosuppressant; anti-inflammatory.
KW
XX
os
    Homo sapiens.
XX
PN
    US6271349-B1.
XX
PD
    07-AUG-2001.
XX
                 98US-00215649.
PF
    17-DEC-1998;
XX
                 96US-0059978P.
PR
    23-DEC-1996;
                 96US-00772330.
PR
    23-DEC-1996;
PR
    07-MAR-1997;
                 97US-0077181P.
PR
    07-MAR-1997;
                 97US-00813509.
PR
    14-OCT-1997;
                 97US-0064671P.
    22-DEC-1997;
                 97US-00996139.
PR
XX
    (IMMV ) IMMUNEX CORP.
PA
XX
PΙ
    Dougall WC, Galibert L;
```

```
XX
DR
    WPI; 1998-377655/32.
DR
    N-PSDB; AAD15311.
XX
    New isolated receptor activator of necrosis factor-kappa B - useful for,
PT
PT
     e.g. developing products for regulating an immune or inflammatory
PT
     response, treating toxic shock or sepsis.
XX
PS
     Example 15; Col 71-72; 47pp; English.
XX
     The patent discloses novel receptor activator of nuclear factor (NF)-
CC
     kappaB (RANK) proteins and their corresponding DNAs. RANK is a member of
CC
     the tumour necrosis factor (TNF) receptor superfamily and associates with
CC
     TNF receptor associated factor (TRAF) 2 and 3 which are important in the
CC
     regulation of immune and inflammatory response. The receptors are useful
CC
     for regulating immune response and in screening for inhibitors of these
CC
     receptors. The cytoplasmic domain of RANK is used in developing assays
CC
CC
     for inhibitors of signal transduction, e.g. for screening the molecules
CC
     that inhibit interaction of RANK with TRAF1, TRAF2, TRAF3, TRAF5 and
     particularly TRAF6. NF-kappaB inhibition by RANK antagonists are useful
CC
     in ameliorating the negative effects of an inflammatory response that
CC
CC
     result from triggering of RANK, e.g. in treating toxic shock or sepsis,
CC
     graft-versus-host reactions, acute inflammatory reactions and the effects
CC
     of bone resorption. RANK acts as an anti- apoptotic signal and rescue the
     cells that express RANK from apoptosis. Soluble forms of the receptor are
CC
CC
     used in vivo or in vitro based screening tests for agonists or
CC
     antagonists of RANK activity, as antagonists of RANK-mediated NF-kappa B
CC
     activation, or to inhibit transduction of a signal via RANK. RANK
     compositions are used in the development of both agonistic and
CC
CC
     antagonistic antibodies, or as an adjunct therapy for disease
CC
     characterised by neoplastic cells that express RANK. Compounds that
CC
     interfere with RANK/TRAF6 interactions are useful for modulating the
CC
     formation of osteoclasts from osteoclast precursors and for modulating
CC
     osteoclast function and activities. They are used as inhibitors of
CC
     diseases associated with excess bone resorption and as immunosuppressants
CC
     or anti-inflammatory agents. The RANK DNAs are useful for the expression
CC
     of recombinant proteins, as probes for analysis of the presence or
CC
     distribution of RANK transcripts, while the proteins are useful in
CC
     preparing kits for the detection of soluble RANK, or monitor RANK-related
CC
     activity. The present sequence is RANK ligand (RANKL) protein from human
XX
SO
     Sequence 317 AA;
  Query Match
                         100.0%;
                                  Score 1685; DB 2; Length 317;
  Best Local Similarity
                         100.0%; Pred. No. 6.2e-154;
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  Matches 317; Conservative
                                0; Mismatches
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              Db
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61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120

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Db

Qу

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Qу
             11111111111111111
         301 PDODATYFGAFKVRDID 317
Db
RESULT 5
AAY84417
    AAY84417 standard; protein; 317 AA.
ID
XX
AC
    AAY84417;
XX
DΤ
    25-JUL-2000 (first entry)
XX
    Amino acid sequence of a human osteoprotegerin ligand (OPGL).
DE
XX
KW
    Osteoprotegerin ligand; OPGL; osteoprotegerin; osteoclastogenesis;
KW
    tumour necrosis factor receptor; type II transmembrane protein;
    osteoclast differentiation; CSF-1; osteoclast activator; immune response;
KW
    osteoporosis; bone resorption.
KW
XX
os
    Homo sapiens.
XX
FH
    Key
                    Location/Qualifiers
FT
    Region
                    49. .69
FT
                    /note= "transmembrane region"
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    Domain
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                    /note= "extracellular stalk domain"
FT
                    158. .317
FT
    Region
\mathbf{FT}
                    /note= "active ligand moiety"
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    WO200015807-A1.
PN
XX
PD
    23-MAR-2000.
XX
                   99WO-DK000481.
PF
    13-SEP-1999;
XX
PR
     15-SEP-1998;
                   98DK-00001164.
                   98US-0102896P.
PR
    02-OCT-1998:
XX
PA
     (MEBI-) M & E BIOTECH AS.
XX
PΙ
    Halkier T, Haaning J;
XX
DR
    WPI; 2000-271444/23.
    N-PSDB; AAZ99964.
DR
XX
     In vivo down-regulation of osteoprotegerin ligand (OPGL) activity used to
PT
```

```
XX
PS
    Claim 19; Page 78-79; 110pp; English.
XX
CC
    The present sequence represents a human osteoprotegerin ligand (OPGL).
CC
    Osteoprotegerin is a secreted member of the tumour necrosis factor
CC
    receptor family, which blocks osteoclastogenesis in a dose dependent
CC
    manner. The OPGL protein is synthesised as a type II transmembrane
    protein. The murine and human OPGL polypeptides are 87% homologous. OPGL
CC
CC
    is a potent osteoclast differentiation factor when combined with CSF-1.
    It is not capable of inducing osteoclast differentiation in the absence
CC
CC
    of CSF-1. OPGL is also an activator of mature osteoclasts. The
CC
    specification describes a method for the in vivo down-regulation of OPGL
CC
    activity in an animal. The method comprises using at least one OPGL
    polypeptide or subsequence, and/or at least one OPGL analogue to induce
CC
    an immune response in the animal. The method and OPGL polypeptide are
CC
    useful for treating, preventing and ameliorating osteoporosis or other
CC
    diseases or conditions characterised by excessive bone resorption
CC
XX
SO
    Sequence 317 AA;
                       100.0%;
 Query Match
                               Score 1685; DB 3;
                                                Length 317;
 Best Local Similarity
                       100.0%;
                               Pred. No. 6.2e-154;
 Matches 317; Conservative
                             0; Mismatches
                                             0; Indels
                                                         0;
                                                             Gaps
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          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qy
            Db
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
         61 VCSVALFFYFRAOMDPNRISEDGTHCIYRILRLHENADFODTTLESQDTKLIPDSCRRIK 120
Qy
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Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
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Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qy
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNODGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
         301 PDQDATYFGAFKVRDID 317
Qу
            111111111
         301 PDODATYFGAFKVRDID 317
Db
RESULT 6
AAE04426
ID
    AAE04426 standard; protein; 317 AA.
XX
AC
    AAE04426;
XX
DT
    04-SEP-2001
                (first entry)
```

treat, prevent and ameliorate osteoporosis.

PT

```
XX
DE
     Human receptor activator of NF-chi B ligand (huRANKL) protein.
XX
KW
     Human; receptor activator of NF-chi B; RANK; tumour necrosis factor; TNF;
KW
     CD40; TNF receptor-associated factor; TRAF; ligand; immune response;
KW
     chromosome 18q22.1; huRANKL; chromosome 13q14; transmembrane protein.
XX
OS
    Homo sapiens.
XX
FH
     Key
                    Location/Qualifiers
FT
     Region
                    162. .317
                    /note= "Receptor binding region"
FT
XX
PN
     US6242213-B1.
XX 、
PD
     05-JUN-2001.
XX
PF
     22-DEC-1997;
                   97US-00995659.
XX
                   96US-0059978P.
PR
    23-DEC-1996;
PR
     23-DEC-1996;
                   96US-00772330.
PR
     07-MAR-1997;
                   97US-0077181P.
     14-OCT-1997;
PR
                   97US-0064671P.
XX
PA
     (IMMV ) IMMUNEX CORP.
XX
PI
    Anderson DM;
XX
DR
    WPI; 2001-407216/43.
DR
    N-PSDB; AAD08715.
XX
PT
    New DNA molecules, useful for producing ligands (which are useful for
PT
    regulating immune response and in screening for inhibitors of NF-chi B
PT
     receptor activator) of the receptor activator of NF-chi B (RANK).
XX
PS
    Claim 1; Col 65-66; 43pp; English.
XX
CC
    The present invention relates to receptor activator of NF-chi B (RANK)
CC
    DNA. RANK is mapped to chromosome 18q22.1 and its ligand (RANKL) to
CC
    chromosome 13q14. RANK and RANKL are type 1 and type 2 transmembrane
CC
    proteins respectively. RANK is a member of the tumour necrosis factor
CC
     (TNF) superfamily and it closely resembles CD40 in the extracellular
CC
     region. RANK associates with TNF receptor-associated factor (TRAF) 2 and
CC
    TRAF3. The DNA molecules are useful for producing ligands of RANK. The
CC
    ligands are useful for regulating immune response and in screening for
CC
    inhibitors of RANK. The present sequence is human RANKL (huRANKL) protein
XX
    Sequence 317 AA;
SO
  Query Match
                         100.0%;
                                  Score 1685; DB 4;
                                                      Length 317;
  Best Local Similarity
                         100.0%;
                                  Pred. No. 6.2e-154;
 Matches 317; Conservative
                                0; Mismatches
                                                  0; Indels
                                                                0;
                                                                            0;
Qy
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
              Db
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
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61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
            Db
         61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
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Qy
            121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qу
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qy
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
         301 PDQDATYFGAFKVRDID 317
Qу
            1111111111111111
         301 PDODATYFGAFKVRDID 317
Db
RESULT 7
AAE01993
    AAE01993 standard; protein; 317 AA.
ID
XX
AC
    AAE01993;
XX
DT
    31-JUL-2001 (first entry)
XX
DE
    Human full-length RANKL (receptor activator of NF-kappaB ligand).
XX
    Human; receptor activator of NF-kappaB; RANK; nuclear factor-kappaB;
KW
    NF-kappaB; tumour necrosis factor; TNF; type I transmembrane protein;
KW
    TNF receptor-associated factor; TRAF; RANK ligand; RANKL; osteopathic;
KW
    inflammatory reaction; bone resorption; gene therapy; immunomodulator;
KW
KW
    immune system dysfunction; familial expansile osteolysis; FEO;
    early onset Paget's disease of bone; EP; cytostatic; chromosome 13q14.
KW
XX
os
    Homo sapiens.
XX
    W0200136637-A1.
PN
XX
    25-MAY-2001.
PD
XX
    14-NOV-2000; 2000WO-US031459.
PF
XX
    17-NOV-1999;
                 99US-00442029.
PR
XX
    (IMMV ) IMMUNEX CORP.
PA
XX
PΙ
    Anderson DM,
                Hughes AE;
XX
DR
    WPI; 2001-329222/34.
DR
    N-PSDB; AAD05904.
XX
    New DNA encoding a receptor activator of NF-kappaB polypeptide for the
PT
    treatment of Pagets disease and Familial Expansile Osteolysis (FEO).
PT
```

```
XX
    Disclosure; Page 76-77; 96pp; English.
PS
XX
CC.
    The present invention relates to a novel receptor, referred to as RANK
CC
    (receptor activator of NF (nuclear factor)-kappaB), a member of TNF
CC
    (tumour necrosis factor) receptor superfamily. RANK is a Type I
CC
    transmembrane protein that interacts with TNF receptor-associated factors
CC
    (TRAFs). Triggering of RANK by overexpression or co-expression of RANK
CC
    and membrane bound RANK ligand (RANKL) results in upregulation of the
CC
    transcription factor NF-kappaB, a ubiquitous transcription factor that is
CC
    most extensively utilised in cells of the immune system. Inhibition of Nf
CC
    -kappaB by RANK antagonists is useful in ameliorating negative effects of
CC
    inflammatory reactions, and the effects of excess bone resorption. The
CC
    RANK DNAs, proteins and their analogues are useful for the preparation of
CC
    pharmaceutical compositions, for infecting target cells for use in gene
CC
    therapy applications in diagnosing diseases associated with RANK, and as
CC
    targets for use in screening assays. They may be used in the treatment or
    diagnosis of immune system dysfunction. The present invention also
CC
CC
    encompasses gene therapy methods to correct gene-activating mutations,
CC
    associated with e.g. familial expansile osteolysis (FEO) and early onset
CC
    Paget's disease of bone (EP). The present amino acid sequence is full-
CC
    length human RANKL (huRANKL) protein. The RANKL gene is located in
CC
    chromosome 13q14
XX
SQ
    Sequence 317 AA;
 Query Match
                       100.0%; Score 1685; DB 4; Length 317;
 Best Local Similarity
                       100.0%; Pred. No. 6.2e-154;
 Matches 317; Conservative
                            0; Mismatches
                                             0; Indels
                                                          0;
                                                             Gaps
                                                                    0;
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
            Db
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qy
         61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qy
            121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qy
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qy
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
```

301 PDQDATYFGAFKVRDID 317

301 PDQDATYFGAFKVRDID 317

Qy

Db

```
ABB08134 standard; protein; 317 AA.
TD
XX
AC
    ABB08134;
XX
DΤ
     10-SEP-2002 (first entry)
XX
DΕ
    Human RANKL polypeptide.
XX
KW
     Dendritic cell; mobilisation factor; T cell; adjuvant; antibacterial;
KW
     fungicide; protozoacide; virucide; anti-inflammatory; anti-HIV;
KW
     tuberculostatic; cytostatic; human; RANKL.
XX
OS
    Homo sapiens.
                                                           (
XX
    WO200236141-A2.
PN
XX
    10-MAY-2002.
PD
XX
    30-OCT-2001; 2001WO-US044834.
PF
XX
    02-NOV-2000; 2000US-0245721P.
PR
XX
PΑ
     (IMMV ) IMMUNEX CORP.
XX
PΙ
    Lynch DH, De Smedt TN, Maliszewski CR, Butz EA, Miller RE;
PΙ
    Thomas EK;
XX
DR
    WPI; 2002-500114/53.
XX
PT
    Treating an individual suffering from infection, e.g. inflammation,
PT
     chickenpox or AIDS, by administering a combination of dendritic cell
PT
    mobilization factor or maturation agent, T cell enhancing factor and
PT
     antigen-specific T cells.
XX
PS
     Disclosure; Page 42-43; 43pp; English.
XX
CC
    The invention relates to treating an individual at risk for or suffering
CC
     from infection with a pathogenic or opportunistic organism. The method
CC
     involves administering a combination of two to five agents comprising:
CC
     (a) dendritic cell mobilisation factor; (b) dendritic cell maturation
CC
     agent; (c) dendritic cell activation agent; (d) T cell enhancing factor;
CC
    or (e) activated, antigen-specific T cells. The methods are useful for
CC
     treating an individual at risk for or suffering from infection with a
CC
    pathogenic or opportunistic organism, e.g. viruses (e.g. HIV), bacteria
CC
     (e.g. M. tuberculosis), yeast, fungi (e.g. C. albicans) or protozoa (e.g.
     T. cruzi, which causes Chaga's disease). The methods are especially
CC
CC
     useful for treating an individual suffering from immunosuppression by
CC
     enhancing a lymphocyte-mediated immune response. In particular, the
CC
    method is useful for treating inflammations, chickenpox, oral or genital
    herpes, mononucleosis, multifocal leukoencephalopathy, hepatitis, AIDS, T
CC
CC
     cell leukemia or T cell lymphoma. The activated antigen-presenting
     dendritic cells are useful as a vaccine adjuvant. The present sequence
CC
CC
     represents a human RANKL polypeptide fragment
XX
SQ
     Sequence 317 AA;
```

```
Best Local Similarity 100.0%; Pred. No. 6.2e-154;
                            0; Mismatches
 Matches 317; Conservative
                                           0; Indels
                                                           Gaps
                                                                  0;
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
            1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHOPPAASRSMFVALLGLGLGQV 60
Db
         61 VCSVALFFYFRAOMDPNRISEDGTHCIYRILRLHENADFODTTLESODTKLIPDSCRRIK 120
QУ
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
        121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
            121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
        181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qy
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
        301 PDODATYFGAFKVRDID 317
Qу
            1111111111111111111
Db
        301 PDQDATYFGAFKVRDID 317
RESULT 9
AAE26103
    AAE26103 standard; protein; 317 AA.
XX
AC
    AAE26103;
XX
DΤ
    14-NOV-2002
               (first entry)
XX
DE-
    Human RANK ligand (RANKL) protein.
XX
KW
    Human; RANK; receptor activator of nuclear factor-kappaB; NF-kB; sepsis;
KW
    immune response; toxic shock; graft-versus-host reaction; therapy; TRAF;
    tumour necrosis factor receptor-associated factor; immunosuppressive;
KW
KW
    antibacterial; antiinflammatory; chromosome 13.
XX
os
    Homo sapiens.
XX
PN
    US2002086827-A1.
XX
PD
    04-JUL-2002.
XX
PF
    30-MAY-2001; 2001US-00871291.
XX
                 96US-0059978P.
PR
    23-DEC-1996;
PR
    07-MAR-1997;
                 97US-0077181P.
PR
    14-OCT-1997;
                 97US-0064671P.
PR
    22-DEC-1997;
                 97US-00996139.
PR
    17-DEC-1999;
                 99US-00466496.
    24-MAY-2000; 2000US-00577800.
PR
```

```
XX
PA
    (IMMV ) IMMUNEX CORP.
XX
PΙ
    Anderson DM;
XX
    WPI; 2002-642254/69.
DR
    N-PSDB; AAD43213.
DR
XX
PΤ
    A novel RANK (receptor activator of nuclear factor-kappaB (NF-kB))
PT
    polypeptide, useful for inhibiting activation of NF-kB and for regulating
    an immune or inflammatory response in an individual.
PT
XX
PS
    Example 15; Page 35; 49pp; English.
XX
CC
    The invention relates to novel RANK (receptor activator of nuclear factor
    -kappaB (NF-kB)) proteins and polynucleotides encoding them. Sequences of
CC
    the invention are useful for inhibiting activation of NF-kappaB. They are
CC
CC
    useful for regulating an immune or inflammatory response in an individual
CC
    at risk for an immune or inflammatory response. Inhibition of NF-kappaB
    by RANK antagonists is useful in ameliorating negative effects of an
CC
    inflammatory response that results from triggering of RANK, for e.g. in
CC
CC
    treating toxic shock or sepsis, graft-versus-host reactions or acute
CC
    inflammatory reactions. Soluble RANK is useful as an adjunct therapy for
CC
    diseases characterised by neoplastic cells that express RANK. Soluble
CC
    forms of the receptor are useful in vitro to screen for agonists or
CC
    antagonists of RANK activity. The cytoplasmic domain of RANK is useful in
CC
    developing assays for inhibitors of signal transduction, to screen for
CC
    molecules that inhibit interaction of RANK with tumour necrosis factor
CC
    receptor-associated factor (TRAF) 2 or TRAF3. The present sequence is
    human RANK ligand (RANKL) protein. RANKL gene is located on chromosome 13
CC
XX
SO
    Sequence 317 AA;
 Query Match
                       100.0%; Score 1685; DB 5;
                                                 Length 317;
 Best Local Similarity
                       100.0%; Pred. No. 6.2e-154;
 Matches 317; Conservative
                             0: Mismatches
                                              0; Indels
                                                              Gaps
                                                                     0;
Qy
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
            1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Db
          61 VCSVALFFYFRAOMDPNRISEDGTHCIYRILRLHENADFODTTLESQDTKLIPDSCRRIK 120
Qy
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 OAFOGAVOKELOHIVGSOHIRAEKAMVDGSWLDLAKRSKLEAOPFAHLTINATDIPSGSH 180
Qy
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Db
Qy
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
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Db
Qу
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
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Db
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301 PDQDATYFGAFKVRDID 317
QУ
              111111111
Db
          301 PDQDATYFGAFKVRDID 317
RESULT 10
ABG31631
     ABG31631 standard; protein; 317 AA.
ID
XX
AC
     ABG31631;
XX
\mathbf{DT}
     29-NOV-2002 (first entry)
XX
DE
     Human RANKL protein.
XX
     Tumour; cancer; dendritic cell mobilisation factor; tumour-killing agent;
KW
     dendritic cell maturation agent; T cell enhancing factor; skin cancer;
KW
     antigen-specific T cell; prostate cancer; liver cancer; bone tumour;
KW
     brain tumour; spinal cord tumour; cervical intraepithelial neoplasia;
KW
     actinic keratosis; dendritic cell maturation stimulator; cytostatic;
KW
     dendritic cell activator; T cell enhancer; human; RANKL.
KW
XX
     Homo sapiens.
OS
XX
PN
     WO200266044-A2.
XX
PD
     29-AUG-2002.
XX
PF
     23-OCT-2001; 2001WO-US046254.
XX
     24-OCT-2000; 2000US-0242868P.
PR
XX
PA
     (IMMV ) IMMUNEX CORP.
XX
PΙ
     Thomas EK, Lyman SD, Lynch DH,
                                       De Smedt TN,
                                                     Maliszewski CR;
XX
DR
     WPI; 2002-674891/72.
XX
     Treating an individual with tumors or cancers, e.g. liver cancer or brain
PΤ
     tumor, by administering a combination of dendritic cell populations, T
PT
     cell enhancing factors and activated, antigen-specific T cells.
PТ
XX
     Disclosure; Page 43-44; 44pp; English.
PS
XX
CC
     The present invention relates to a new method for treating a tumour-
CC
     bearing subject. The method involves administering a combination of 2 to
     5 agents comprising dendritic cell mobilisation factor, dendritic cell
CC
     maturation agent, tumour-killing agent, T cell enhancing factor or
CC
CC
     activated, antigen-specific T cells. The method is useful for treating
     tumours or cancers in a subject e.g. skin cancer, prostate cancer, liver
CC
     cancer, tumours of the bone, brain or spinal cord, actinic keratosis, or
CC
     cervical intraepithelial neoplasia. The present amino acid sequence
CC
CC
     represents the human RANKL protein that was used in the method of the
CC
     invention
```

XX SQ

Sequence 317 AA;

```
Query Match
                       100.0%; Score 1685; DB 5; Length 317;
  Best Local Similarity
                       100.0%;
                               Pred. No. 6.2e-154;
 Matches 317; Conservative
                             0; Mismatches
                                             0;
                                                            Gaps
                                               Indels
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Qу
            Db
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Qу
            Db
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         121 QAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
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Qу
            Db
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            11111111111111111
Db
         301 PDQDATYFGAFKVRDID 317
RESULT 11
AAU78285
ID
    AAU78285 standard; protein; 317 AA.
XX
AC
    AAU78285;
XX
DΤ
    18-JUN-2002 (first entry)
XX
DE
    Human TRANCE protein splice variant 1.
XX
KW
    Human; tumour necrosis factor-related activation induced cytokine;
    TRANCE; dwarfism; osteopetrosis; craniofacial-skeletal discrepancy;
KW
    bone damage; cartilage damage; traumatic injury; surgery; osteoarthritis;
KW
    rheumatoid arthritis; acromegaly; gigantism; exostosis; carilaginea;
KW
    exostosis bursata; multiple osteocartilaginous exostosis; chondrocyte;
KW
KW
    cartilage growth; skeletal growth.
XX
    Homo sapiens.
OS
XX
FH
                  Location/Qualifiers
    Key
FT
    Region
                  126. .317
                  /note= "Specifically claimed in claims 17 and 18"
FT
FT
    Region
                  137. .317
FT
                  /note= "Specifically claimed in claims 17 and 18"
FT
                  140. .317
    Region
FT
                  /note= "Specifically claimed in claims 17 and 18"
FT
                  145. .317
    Region
FT
                  /note= "Specifically claimed in claims 17 and 18"
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158. .317
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FT
FT
     Domain
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FТ
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XX
    WO200216551-A2.
PN
XX
    28-FEB-2002.
PD
XX
    20-AUG-2001; 2001WO-US026101.
PF
XX
    18-AUG-2000; 2000US-0226197P.
PR
XX
     (UYMA-) UNIV MASSACHUSETTS MEDICAL CENT.
PA
XX
    Choi Y, Odgren PR, Marks SC;
PΙ
XX
DR
    WPI; 2002-304119/34.
    N-PSDB; ABK12876.
DR
XX
PT
    Treating mammal having disorder characterized by abnormal
     cartilage/skeletal growth such as dwarfism, acromegaly, by administering
PT
PT
    tumor necrosis factor-related activation induced cytokine-modulating
PT
    agent to mammal.
XX
PS
    Disclosure; Fig 10; 55pp; English.
XX
CC
    The present invention relates to a new method of treating a mammal having
CC
     a disorder comprising insufficient or excessive cartilage or skeletal
    growth. The method of the invention involves administering to the mammal
CC
     a tumour necrosis factor-related activation induced cytokine (TRANCE)-
CC
    modulating agent. The method is useful for treating a mammal having a
CC
CÇ
    disorder comprising insufficient or excessive cartilage or skeletal
CC
     growth, where the disorder comprising insufficient cartilage or skeletal
    growth is selected from dwarfism, osteopetrosis, craniofacial-skeletal
CC
CC
    discrepancies and bone or cartilage damage resulting from traumatic
     injury, surgery, osteoarthritis or rheumatoid arthritis, and disorders
CC
     comprising excessive cartilage or skeletal growth are selected from
CC
CC
     acromegaly, gigantism, exostosis, carilaginea, exostosis bursata and
    multiple osteocartilaginous exostoses. The method is useful for
CC
     inhibiting chondrocyte differentiation. The present amino acid sequence
CC
     represents the human TRANCE protein, splice variant 1, of the invention.
CC
CC
    TRANCE is a member of the tumour necrosis factor family and acts directly
CC
    on cartilage-producing cells (chondrocytes)
XX
SO
    Sequence 317 AA;
  Query Match
                         100.0%; Score 1685; DB 5;
                                                      Length 317;
  Best Local Similarity
                         100.0%;
                                  Pred. No. 6.2e-154;
 Matches 317; Conservative
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Db
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ID
XX
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AC
XX
DT
    22-NOV-2002 (first entry)
XX
    C neoformans antigen expressing dendritic cell related protein #5.
DE
XX
KW
    Human; fungicide; fungal infection; dendritic cell; antigen;
    Cryptococcus neoformans; vaccine; immunostimulant.
KW
XX
OS
    Homo sapiens.
XX
    WO200266053-A2.
PN
XX
    29-AUG-2002.
PD
XX
    14-DEC-2001; 2001WO-US048288.
PF
XX
    04-JAN-2001; 2001US-0259653P.
PR
XX
    (IMMV ) IMMUNEX CORP.
PA
XX
PΙ
    Thomas EK;
XX
    WPI; 2002-674896/72.
DR
XX
    Producing a population of activated, Cryptococcus neoformans antigen-
PT
    presenting dendritic cells for preventing or treating C. neoformans
    infection comprises causing the obtained dendritic cells to present the
РΤ
PT
    antigen.
XX
PS
    Disclosure; Page 30-32; 32pp; English.
XX
    The present invention relates to a method of producing a population of
CC
```

```
activated, Cryptococcus neoformans antigen-presenting dendritic cells,
CC
    comprising causing the obtained dendritic cells to present the antigen
CC
    and maturing the dendritic cells. The activated, C. neoformans antigen-
CC
    expressing dendritic cells are useful for treating, or as vaccines or
CC
    vaccine adjuvants against, C. neoformans infection, or for generating
CC
    antigen-specific T cells. The present sequence is a human protein shown
CC
    in the exemplification of the invention
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                      100.0%; Score 1685; DB 5; Length 317;
 Query Match
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XX
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AC
XX
    05-FEB-2003 (first entry)
DT
XX
DE
    Human osteoprotegerin ligand.
XX
    Osteoprotegerin ligand; OPG ligand; OPGL; human; autoimmune disease;
KW
    rheumatoid arthritis; diabetes; osteoarthritis; psoriasis;
KW
    inflammatory bowel disease; transplant rejection; allergy;
KW
KW
    immunosuppressive; antirheumatic; antiarthritic; antidiabetic;
KW
    antipsoriatic; immunosuppressive; antiallergic; antiinflammatory;
KW
    osteopathic; antiulcer; monocyte.
XX
os
    Homo sapiens.
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CC

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XX
     06-FEB-2002; 2002WO-US001238.
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PR
     23-MAR-2001; 2001US-0278215P.
XX
PA
     (GETH ) GENENTECH INC.
XX
PΙ
     Grewal I;
XX
DR
     WPI; 2003-058352/05.
DR
     N-PSDB; ABV75842.
XX
PT
     Stimulating mammalian monocytes by exposing to an OPG ligand polypeptide,
PT
     useful for treating immune related disorders such as autoimmune disease,
PT
     rheumatoid arthritis, diabetes, osteoarthritis, psoriasis, and allergy.
XX
PS
     Claim 1; Fig 1B; 111pp; English.
XX
CC
     The present sequence is the protein sequence of human osteoprotegerin
CC
     ligand (OPGL), a member of the tumour necrosis factor (TNF) family of
CC
CC
     and OPG. In the present invention, OPGL was shown to activate human
CC
CC
    chemokines such as IL-8. OPGL may function in up-regulation of co-
CC
CC
```

molecules that has been reported to bind to at least 2 receptors, RANK monocytes, and to activate such monocytes to secrete certain cytokines such as interleukin-1 (IL-1), IL-6, IL-12, MIP-lalpha and TNF-alpha and stimulatory molecules such as ICAM-a and VCAM-1, LFA, and B7.1, B7.3 and B7h. OPGL may also serve as an antigen presenting molecule which enhances T-cell activation. The invention provides methods of using OPGL to activate monocytes to secrete chemokines or cytokines by exposing a mammalian cell (in cell culture or in a mammal) to OPGL. Also provided are methods of using OPGL to treat conditions or diseases in mammals associated with, or resulting from lack of, or decreased, chemokine or cytokine secretion by monocytes. The invention also provides agonist and antagonist molecules to modulate immune activity. These may include antibodies to the OPG or RANK receptors. An antagonist comprising an anti -OPGL antibody, an anti-OPG receptor antibody, an anti-RANK receptor antibody, an OPG receptor immunoadhesin or a RANK receptor immunoadhesin is used in a claimed method of treating an immune-related condition, especially an autoimmune disease, rheumatoid arthritis, insulin dependent diabetes, osteoarthritis, inflammatory bowel disease (especially ulcerative colitis or Crohn's disease), psoriasis, transplant rejection

CC

```
CC
    or allergy
XX
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 Query Match
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XX
AC
    AAE34364;
XX
DT
    14-MAY-2003 (first entry)
XX
    Human receptor activator of NF-kappa B ligand (RANKL).
DE
XX
    Human; acute septic arthritis; osteomalacia; hyperparathyroidism;
KW
KW
    Cushing's syndrome; receptor activator of NF-kappa B ligand; cancer;
    bone formation; rickets; Langerhan's cell histiocytosis; gene therapy;
KW
    monoostotic fibrous dysplasia; radiation therapy; spinal cord injury;
KW
    RANKL; Gaucher's disease; polyostotic fibrous dysplasia; scurvy.
KW
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OS
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XX
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XX
ΡF
     17-MAY-2002; 2002WO-US016002.
XX
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PR
XX
     (IMMV ) IMMUNEX CORP.
PA
XX
PΙ
    Dougall WC, Anderson DM;
XX
    WPI; 2003-129220/12.
DR
DR
    N-PSDB; AAD52598.
XX
PΤ
     Treating patients having e.g. acute septic arthritis, osteomalacia,
PT
     hyperparathyroidism, Cushing's syndrome or spinal cord injury, comprises
     administering a receptor activator of NF-kappa B antagonist to increase
PT
PT
    bone formation.
XX
PS
     Claim 1; Page 51-52; 52pp; English.
XX
CC
     The invention relates to a method of treating a patient having e.g. acute
CC
     septic arthritis, osteomalacia, hyperparathyroidism, Cushing's syndrome
CC
     or spinal cord injury. The method involves administering a receptor
CC
     activator of NF-kappa B (RANK) antagonist to stimulate an increase in the
CC
     rate for formation of new bone. RANK antagonist is capable of inhibiting
     the ability of RANK to induce NF-kappa B. The method is useful for
CC
    stimulating bone formation, or for treating patients having acute septic
CC
CC
     arthritis, osteomalacia (including rickets and scurvy),
CC
    hyperparathyroidism, Cushing's syndrome, monoostotic fibrous dysplasia,
CC
     polyostotic fibrous dysplasia, Gaucher's disease, Langerhan's cell
CC
    histiocytosis, spinal cord injury, patients requiring periodontal
CC
     reconstruction, or patients who have completed a course or radiation
CC
     therapy for cancer. The method is also useful for treating a patient who
CC
     is a prosthetic joint recipient, a bone graft recipient, or a ligament
CC
     graft recipient. The invention is useful in gene therapy. The present
CC
     sequence is human RANK ligand (RANKL) protein
XX
SO
    Sequence 317 AA;
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                                 Score 1685; DB 6; Length 317;
  Best Local Similarity
                         100.0%;
                                 Pred. No. 6.2e-154;
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ID
XX
AC
    ABR42314;
XX
\mathbf{DT}
    11-AUG-2003 (first entry)
XX
DE
    Human RANKL protein.
XX
KW
    Human; RANKL; tumour necrosis factor; ligand; cytostatic;
KW
    immunomodulator; osteopathic.
XX
os
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XX
    WO2003040307-A2.
PN
XX
PD
    15-MAY-2003.
XX
PF
    25-JUL-2002; 2002WO-US023782.
XX
    27-JUL-2001; 2001US-0307838P.
PR
XX
    (HUMA-) HUMAN GENOME SCI INC.
PA
XX
PΙ
    Hilbert DH, Rosen CA;
XX
    WPI; 2003-430659/40.
DR
XX
    New heteromultimeric complex having a first polypeptide member of the
PТ
    tumor necrosis factor (TNF) ligand family, and a second different member
PΤ
    of TNF ligand family, useful for treating cancer, osteoporosis or an
PΤ
PT
    autoimmune disease.
XX
    Disclosure; Page 366-367; 388pp; English.
PS
XX
CC
    The present sequence is the protein sequence of human RANKL protein. The
    invention relates to compositions comprising heterotrimeric complexes of
CC
    tumour necrosis factor (TNF) ligand family members, and their use in the
CC
    detection, prevention and treatment of disease. In one embodiment, the
CC
```

```
heterotrimeric complex comprises full-length or extracellular portions of
CC
    RANKL and full-length or extracellular portions of other TNF ligand
CC
    family members, preferably TRAIL. The heterotrimeric complexes of the
CC
    invention are useful for treating an autoimmune disease, cancer or
CC
    osteoporosis, and particularly for inhibiting cancer cell proliferation,
CC
    increasing B cell proliferation, or inducing apoptosis of T cells. A
CC
    claimed method of inhibiting cancer cell proliferation comprises
CC
    administering a heterotrimeric complex consisting of TRAIL and CD40L or
CC
    RANKL. A claimed method of treating osteoporosis comprises administering
CC
    an antibody against a complex comprising RANKL and TRAIL
XX
SQ
    Sequence 317 AA;
 Query Match
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                             Score 1685; DB 6; Length 317;
 Best Local Similarity
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CC

## GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: November 8, 2004, 18:26:09; Search time 40 Seconds

(without alignments)

525.570 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

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Total number of hits satisfying chosen parameters: 478139

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

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Listing first 45 summaries

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#### SUMMARIES

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	3	1685	100.0	317	3	US-09-215-649A-13	Sequence 13, Appl
	4	1685	100.0	317	3	US-09-052-521C-4	Sequence 4, Appli
	5	1685	100.0	317	4	US-09-577-780-13	Sequence 13, Appl
	6	1685	100.0	317	4	US-09-577-800-13	Sequence 13, Appl
	7	1685	100.0	317	4	US-09-466-496-13	Sequence 13, Appl
	8	1685	100.0	317	4	US-09-871-856-13	Sequence 13, Appl
	9	1685	100.0	317	4	US-09-871-291-13	Sequence 13, Appl
	10	1685	100.0	317	4	US-09-396-937-2	Sequence 2, Appli
	11	1685	100.0	317	4	US-09-877-650-13	Sequence 13, Appl

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#### ALIGNMENTS

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; Patent No. 6017729
  GENERAL INFORMATION:
    APPLICANT: Anderson, Dirk M.
    APPLICANT: Galibert, Laurent
;
    APPLICANT: Maraskovsky, Eugene
    TITLE OF INVENTION: Receptor Activator of NF-kappaB
;
    NUMBER OF SEQUENCES: 19
    CORRESPONDENCE ADDRESS:
      ADDRESSEE:
                  Immunex Corporation, Law Department
       STREET: 51 University Street
      CITY: Seattle
      STATE: WA
      COUNTRY: USA
;
       ZIP: 98101
    COMPUTER READABLE FORM:
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MEDIUM TYPE: Floppy disk
      COMPUTER: Apple Power Macintosh
      OPERATING SYSTEM: Apple Operating System 7.5.5
      SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
    CURRENT APPLICATION DATA:
      APPLICATION NUMBER: US/08/996,139
      FILING DATE: 22 DECEMBER 1997
      CLASSIFICATION:
    PRIOR APPLICATION DATA:
     APPLICATION NUMBER: USSN 60/064,671
      FILING DATE: 14 OCTOBER 1997
    PRIOR APPLICATION DATA:
     APPLICATION NUMBER: USSN 08/813,509
      FILING DATE: 07 MARCH 1997
    PRIOR APPLICATION DATA:
     APPLICATION NUMBER: USSN 08/772,330
     FILING DATE: 23 DECEMBER 1996
    ATTORNEY/AGENT INFORMATION:
     NAME: Perkins, Patricia Anne
     REGISTRATION NUMBER: 34,693
      REFERENCE/DOCKET NUMBER:
                            2851-A
    TELECOMMUNICATION INFORMATION:
      TELEPHONE: (206) 587-0430
      TELEFAX: (206)233-0644
  INFORMATION FOR SEQ ID NO: 13:
    SEQUENCE CHARACTERISTICS:
     LENGTH: 317 amino acids
      TYPE: amino acid
      TOPOLOGY: linear
    MOLECULE TYPE: protein
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US-08-995-659-13

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; Patent No. 6242213
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    APPLICANT: Anderson, Dirk M.
    APPLICANT: Galibert, Laurent
    APPLICANT: Maraskovsky, Eugene
    TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
    NUMBER OF SEQUENCES: 19
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: Immunex Corporation, Law Department
       STREET: 51 University Street
      CITY: Seattle
      STATE: WA
      COUNTRY: USA
       ZIP: 98101
    COMPUTER READABLE FORM:
      MEDIUM TYPE: Floppy disk
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       FILING DATE: 14 OCTOBER 1997
       CLASSIFICATION:
    PRIOR APPLICATION DATA:
      APPLICATION NUMBER: USSN 08/813,509
      FILING DATE: 07 MARCH 1997
      CLASSIFICATION:
    PRIOR APPLICATION DATA:
      APPLICATION NUMBER: USSN 08/772,330
      FILING DATE: 23 DECEMBER 1996
      CLASSIFICATION:
    ATTORNEY/AGENT INFORMATION:
      NAME: Perkins, Patricia Anne
      REGISTRATION NUMBER: 34,693
      REFERENCE/DOCKET NUMBER: 2852-A
     TELECOMMUNICATION INFORMATION:
      TELEPHONE: (206) 587-0430
       TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
    SEQUENCE CHARACTERISTICS:
       LENGTH: 317 amino acids
       TYPE: amino acid
      TOPOLOGY: linear
    MOLECULE TYPE: protein
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       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
           ADDRESSEE: Immunex Corporation, Law Department
           STREET: 51 University Street
           CITY: Seattle
            STATE: WA
           COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
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            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
           NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 317 amino acids
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; Patent No. 6316408
; GENERAL INFORMATION:
  APPLICANT: Boyle, William J.
  TITLE OF INVENTION: Osteoprotegerin Binding Proteins and Receptors
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  CURRENT FILING DATE: 1998-03-30
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  PRIOR FILING DATE: 1997-06-23
  PRIOR APPLICATION NUMBER: 08/842,842
  PRIOR FILING DATE: 1997-04-16
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       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                Maraskovsky, Eugene
       TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
           ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
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CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
        COMPUTER READABLE FORM:
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            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
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            CLASSIFICATION: <Unknown>
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            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2852-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
        SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
       MOLECULE TYPE: protein
        SEQUENCE DESCRIPTION: SEQ ID NO: 13:
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                      100.0%; Pred. No. 3.7e-163;
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; Patent No. 6479635
  GENERAL INFORMATION:
    APPLICANT: Anderson, Dirk M.
    APPLICANT: Galibert, Laurent
    APPLICANT: Maraskovsky, Eugene
    TITLE OF INVENTION: Receptor Activator of NF-kappaB
    NUMBER OF SEQUENCES: 19
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: Immunex Corporation, Law Department
      STREET: 51 University Street
      CITY: Seattle
      STATE: WA
      COUNTRY: USA
      ZIP: 98101
    COMPUTER READABLE FORM:
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      FILING DATE: 22 DECEMBER 1997
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      APPLICATION NUMBER: USSN 60/064,671
      FILING DATE: 14 OCTOBER 1997
    PRIOR APPLICATION DATA:
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      FILING DATE: 07 MARCH 1997
    PRIOR APPLICATION DATA:
      APPLICATION NUMBER: USSN 08/772,330
      FILING DATE: 23 DECEMBER 1996
    ATTORNEY/AGENT INFORMATION:
      NAME: Perkins, Patricia Anne
      REGISTRATION NUMBER: 34,693
      REFERENCE/DOCKET NUMBER: 2851-A
    TELECOMMUNICATION INFORMATION:
      TELEPHONE: (206) 587-0430
      TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
;
    SEQUENCE CHARACTERISTICS:
      LENGTH: 317 amino acids
      TYPE: amino acid
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TOPOLOGY: linear
    MOLECULE TYPE: protein
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 Query Match
                      100.0%; Score 1685; DB 4;
                                              Length 317;
 Best Local Similarity
                      100.0%; Pred. No. 3.7e-163;
 Matches 317; Conservative
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 Patent No. 6528482
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
;
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
;
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
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            APPLICATION NUMBER: USSN 60/064,671
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            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206) 233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
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            TYPE: amino acid
            TOPOLOGY: linear
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Qу
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
Qу
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            Db
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        301 PDODATYFGAFKVRDID 317
            11111111111111
Db
        301 PDQDATYFGAFKVRDID 317
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US-09-871-856-13
; Sequence 13, Application US/09871856
; Patent No. 6537763
   GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
                   Galibert, Laurent
                   Maraskovsky, Eugene
        TITLE OF INVENTION: Receptor Activator of NF-kappaB
        NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: Immunex Corporation, Law Department
             STREET: 51 University Street
             CITY: Seattle
             STATE: WA
             COUNTRY: USA
             ZIP: 98101
        COMPUTER READABLE FORM:
             MEDIUM TYPE: Floppy disk
             COMPUTER: Apple Power Macintosh
             OPERATING SYSTEM: Apple Operating System 7.5.5
             SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
        CURRENT APPLICATION DATA:
             APPLICATION NUMBER: US/09/871,856
             FILING DATE: 31-May-2001
             CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
             APPLICATION NUMBER: 08/996,139
             FILING DATE: <Unknown>
             APPLICATION NUMBER: USSN 08/813,509
             FILING DATE: 07 MARCH 1997
             APPLICATION NUMBER: USSN 08/772,330
             FILING DATE: 23 DECEMBER 1996
        ATTORNEY/AGENT INFORMATION:
             NAME: Perkins, Patricia Anne
             REGISTRATION NUMBER: 34,693
             REFERENCE/DOCKET NUMBER: 2851-A
        TELECOMMUNICATION INFORMATION:
             TELEPHONE: (206) 587-0430
             TELEFAX: (206)233-0644
    INFORMATION FOR SEQ ID NO: 13:
        SEQUENCE CHARACTERISTICS:
             LENGTH: 317 amino acids
             TYPE: amino acid
             TOPOLOGY: linear
        MOLECULE TYPE: protein
        SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-871-856-13
 Query Match
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                                                     Length 317;
 Best Local Similarity
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 Matches 317; Conservative
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Db
         301 PDQDATYFGAFKVRDID 317
QУ
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         301 PDQDATYFGAFKVRDID 317
Db
RESULT 9
US-09-871-291-13
; Sequence 13, Application US/09871291
; Patent No. 6562948
   GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
;
                 Maraskovsky, Eugene
        TITLE OF INVENTION: Receptor Activator of NF-kappaB
;
        NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
        COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
        CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/871,291
            FILING DATE: 30-May-2001
            CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
            APPLICATION NUMBER: 08/996,139
            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
        ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
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TELECOMMUNICATION INFORMATION:
           TELEPHONE: (206) 587-0430
           TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 317 amino acids
           TYPE: amino acid
           TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-871-291-13
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                      100.0%; Pred. No. 3.7e-163;
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Qу
            301 PDQDATYFGAFKVRDID 317
Db
RESULT 10
US-09-396-937-2
; Sequence 2, Application US/09396937
: Patent No. 6645500
: GENERAL INFORMATION:
  APPLICANT: M&E Biotech A/S
  APPLICANT: HALKIER, Torben
  APPLICANT: HAANING, Jesper
  TITLE OF INVENTION: Method for Down-Regulating Osteoprotegerin Ligand
  TITLE OF INVENTION: Activity
  FILE REFERENCE: 22021 PC 1
  CURRENT APPLICATION NUMBER: US/09/396,937
  CURRENT FILING DATE: 1999-09-15
  NUMBER OF SEQ ID NOS: 35
  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 2
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   ORGANISM: Homo sapiens
US-09-396-937-2
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Db
        241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
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        301 PDQDATYFGAFKVRDID 317
Qу
            111111111111111111
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RESULT 11
US-09-877-650-13
; Sequence 13, Application US/09877650
 Patent No. 6649164
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
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           FILING DATE: 08-Jun-2001
           CLASSIFICATION: <Unknown>
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           APPLICATION NUMBER: 08/995,659
           FILING DATE: 1997-12-22
           APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
           APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
           NAME: Perkins, Patricia Anne
           REGISTRATION NUMBER: 34,693
           REFERENCE/DOCKET NUMBER: 2852-A
       TELECOMMUNICATION INFORMATION:
           TELEPHONE: (206) 587-0430
           TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
           LENGTH: 317 amino acids
           TYPE: amino acid
           TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-877-650-13
 Query Match
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                             Score 1685; DB 4; Length 317;
 Best Local Similarity
                      100.0%; Pred. No. 3.7e-163;
 Matches 317; Conservative
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RESULT 12 US-09-865-363-13

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; Sequence 13, Application US/09865363
 Patent No. 6740522
   GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
                  Galibert, Laurent
                  Maraskovsky, Eugene
        TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
        NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: Immunex Corporation, Law Department
             STREET: 51 University Street
            CITY: Seattle
             STATE: WA
            COUNTRY: USA
            ZIP: 98101
        COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
             COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
             SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
        CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/865,363
             FILING DATE: 25-May-2001
             CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
            APPLICATION NUMBER: 08/995,659
            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
             FILING DATE: 07 MARCH 1997
             APPLICATION NUMBER: USSN 08/772,330
             FILING DATE: 23 DECEMBER 1996
        ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
             REGISTRATION NUMBER: 34,693
             REFERENCE/DOCKET NUMBER: 2852-A
        TELECOMMUNICATION INFORMATION:
             TELEPHONE: (206) 587-0430
             TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
        SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
             TYPE: amino acid
             TOPOLOGY: linear
        MOLECULE TYPE: protein
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US-09-865-363-13
 Query Match
                        100.0%; Score 1685; DB 4; Length 317;
 Best Local Similarity
                        100.0%; Pred. No. 3.7e-163;
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Qу
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Db
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            Db
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RESULT 13
US-08-842-842-7
; Sequence 7, Application US/08842842
; Patent No. 5843678
  GENERAL INFORMATION:
    APPLICANT: Boyle, William J.
    TITLE OF INVENTION: OSTEOPROTEGERIN BINDING PROTEINS
    NUMBER OF SEQUENCES: 7
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: Amgen Inc.
      STREET: 1840 Dehavilland Drive
      CITY: Thousand Oaks
      STATE: California
      COUNTRY: USA
      ZIP: 91230-1789
    COMPUTER READABLE FORM:
      MEDIUM TYPE: Floppy disk
      COMPUTER: IBM PC compatible
      OPERATING SYSTEM: PC-DOS/MS-DOS
      SOFTWARE: PatentIn Release #1.0, Version #1.30
    CURRENT APPLICATION DATA:
     APPLICATION NUMBER: US/08/842,842
      FILING DATE:
      CLASSIFICATION: 435
    ATTORNEY/AGENT INFORMATION:
      NAME: Winter, Robert B.
      REFERENCE/DOCKET NUMBER: A-451
  INFORMATION FOR SEQ ID NO: 7:
    SEQUENCE CHARACTERISTICS:
      LENGTH: 316 amino acids
      TYPE: amino acid
      TOPOLOGY: linear
    MOLECULE TYPE: protein
US-08-842-842-7
 Query Match
                       84.1%; Score 1417.5; DB 2; Length 316;
 Best Local Similarity 84.3%; Pred. No. 6.6e-136;
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 Matches 268; Conservative 16; Mismatches
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RESULT 14
US-08-989-362-2
; Sequence 2, Application US/08989362
; Patent No. 6242586
  GENERAL INFORMATION:
    APPLICANT: Gorman, Daniel M.
    APPLICANT: Mattson, Jeanine D.
    TITLE OF INVENTION: Mammalian Cell Surface Antigens; Related
    TITLE OF INVENTION: Reagents
    NUMBER OF SEQUENCES: 2
    CORRESPONDENCE ADDRESS:
      ADDRESSEE: DNAX Research Institute
      STREET: 901 California Avenue
      CITY: Palo Alto
      STATE: California
      COUNTRY: USA
      ZIP: 94304-1104
    COMPUTER READABLE FORM:
      MEDIUM TYPE: Floppy disk
      COMPUTER: IBM PC compatible
      OPERATING SYSTEM: PC-DOS/MS-DOS
      SOFTWARE: PatentIn Release #1.0, Version #1.30
    CURRENT APPLICATION DATA:
      APPLICATION NUMBER: US/08/989,362
      FILING DATE:
                 12-DEC-1997
      CLASSIFICATION: 56
    PRIOR APPLICATION DATA:
      APPLICATION NUMBER: US 60/032,846
      FILING DATE: 13-DEC-1996
    ATTORNEY/AGENT INFORMATION:
      NAME: Ching, Edwin P.
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REFERENCE/DOCKET NUMBER: DX0686
    TELECOMMUNICATION INFORMATION:
     TELEPHONE:
                (650)852-9196
     TELEFAX: (650)496-1204
  INFORMATION FOR SEQ ID NO: 2:
    SEQUENCE CHARACTERISTICS:
     LENGTH: 316 amino acids
     TYPE: amino acid
     TOPOLOGY: linear
    MOLECULE TYPE: protein
US-08-989-362-2
                      84.1%; Score 1417.5; DB 3; Length 316;
 Query Match
                      84.3%; Pred. No. 6.6e-136;
 Best Local Similarity
 Matches 268; Conservative 16; Mismatches
                                                                  2;
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                                               Indels
                                                           Gaps
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Db
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Qу
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Db
RESULT 15
US-09-052-521C-2
; Sequence 2, Application US/09052521C
; Patent No. 6316408
; GENERAL INFORMATION:
  APPLICANT: Boyle, William J.
  TITLE OF INVENTION: Osteoprotegerin Binding Proteins and Receptors
  FILE REFERENCE: A-451Brv
  CURRENT APPLICATION NUMBER: US/09/052,521C
  CURRENT FILING DATE: 1998-03-30
  PRIOR APPLICATION NUMBER: 08/880,855
  PRIOR FILING DATE: 1997-06-23
  PRIOR APPLICATION NUMBER: 08/842,842
  PRIOR FILING DATE: 1997-04-16
  NUMBER OF SEQ ID NOS: 40
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REGISTRATION NUMBER: 34,090

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   ORGANISM: Mouse
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                    84.1%; Score 1417.5; DB 3; Length 316;
 Query Match
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 Matches 268; Conservative 16; Mismatches
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Db
       120 KQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGS 179
Qу
                              119 KQAFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQRGKPEAQPFAHLTINAASIPSGS 178
Db
       180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
Qу
           Db
       179 HKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLM 238
       240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
Qy
           Db
       239 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLL 298
       300 DPDQDATYFGAFKVRDID 317
Qу
           11111111111111111111
       299 DPDQDATYFGAFKVQDID 316
Db
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Search completed: November 8, 2004, 18:41:01 Job time: 42 secs

### GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: November 8, 2004, 18:15:11; Search time 39 Seconds

(without alignments)

782.070 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

Sequence: 1 MRRASRDYTKYLRGSEEMGG.....LLDPDQDATYFGAFKVRDID 317

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 283416 seqs, 96216763 residues

Total number of hits satisfying chosen parameters: 283416

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database: PIR\_79:\*

1: pir1:\*

2: pir2:\*

3: pir3:\*

4: pir4:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

		8				
Result		Query				
No.	Score	Match	Length	DB	ID .	Description
1	189	11.2	281	2	 I38 <b>7</b> 07	Fas ligand - human
2	184.5	10.9	279	2	A53062	Fas ligand - mouse
3	176.5	10.5	261	2	s53090	CD40 ligand - bovi
4	175.5	10.4	278	2	A49266	fas ligand - rat
5	158.5	9.4	261	2	I53476	CD40 ligand - huma
6	141.5	8.4	235	1	QWMSN	tumor necrosis fac
7	141	8.4	234	1	A25451	tumor necrosis fac
8	137	8.1	234	1	JH0529	tumor necrosis fac
9	133	7.9	233	1	QWHUN	tumor necrosis fac
10	132.5	7.9	235	2	I54490	tumor necrosis fac
11	131.5	7.8	235	2	JU0029	tumor necrosis fac
12	130.5	7.7	306	2	I49139	lymphotoxin-beta -
13	130	7.7	233	1	S22052	tumor necrosis fac

14	128	7.6	234	1	JQ1344	tumor necrosis fac
15	126.5	7.5	233	1	S24642	tumor necrosis fac
16	126	7.5	232	1	S12606	tumor necrosis fac
17	125.5	7.4	185	2	S52715	tumor necrosis fac
18	122	7.2	193	2	S06192	tumor necrosis fac
19	120	7.1	260	2	S21738	CD40 ligand - mous
20 -	117	6.9	233	2	S11688	tumor necrosis fac
21	117	6.9	244	2	A46066	lymphotoxin beta -
22	97.5	5.8	1464	1	CGHU1S	collagen alpha 1(I
.23	94.5	5.6	664	2	C84747	probable protein k
24	92.5	5.5	205	1	QWHUX	lymphotoxin alpha
25	92.5	5.5	450	2	S38114	hypothetical prote
26	91.5	5.4	3848	2	T17414	TipC protein - sli
27	91	5.4	493	2	AC0937	probable GntR-fami
28	90.5	5.4	1694	2	S50065	sialoadhesin - mou
29	90	5.3	730	2	JC1456	gelatinase B (EC 3
30	89.5	5.3	331	2	AF3526	homoprotocatechuat
31	89.5	5.3	379	2	A47659	farnesyl-protein t
32	89	5.3	202	1	B27303	tumor necrosis fac
33	89	5.3	440	2	I49681	glyceraldehyde-3-p
34	89	5.3	479	2	A25052	fibrinogen beta ch
35	89	5.3	639	2	C83624	probable two-compo
36	88.5	5.3	565	2	C89893	hypothetical prote
37	88.5	5.3	578	2	S51379	probable phosphoes
38	88.5	5.3	684	2	T01267	leucine-rich repea
39	88.5	5.3	883	2	A49733	[heparan sulfate]-
40	87.5	5.2	610	2	т06690	galactonolactone d
41	87.5	5.2	1466	1	CGHU7L	collagen alpha 1(I
42	87	5.2	639	2	A32935	protein P1 - Entam
43	87	5.2	1114	2	JH0284	125K surface antig
44	87	5.2	1315	2	G96722	hypothetical prote
45	86.5	5.1	279	2	F72339	hypothetical prote

#### ALIGNMENTS

### RESULT 1 I38707

Fas ligand - human

C; Species: Homo sapiens (man)

C;Date: 29-May-1998 #sequence\_revision 29-May-1998 #text\_change 09-Jul-2004

C; Accession: I38707; JC2340; S57565; I38554

R; Takahashi, T.; Tanaka, M.; Inazawa, J.; Abe, T.; Suda, T.; Nagata, S.

Int. Immunol. 6, 1567-1574, 1994

A;Title: Human Fas ligand: gene structure, chromosomal location and species specificity.

A; Reference number: I38707; MUID: 95127560; PMID: 7826947

A; Accession: I38707

A; Status: preliminary; translated from GB/EMBL/DDBJ

A; Molecule type: mRNA A; Residues: 1-281 < RES>

A;Cross-references: UNIPROT:P48023; EMBL:U11821; NID:g595430; PIDN:AAC50124.1;

PID:g595431

R; Mita, E.; Hayashi, N.; Iio, S.; Takehara, T.; Hijioka, T.; Kasahara, A.;

Fusamoto, H.; Kamada, T.

Biochem. Biophys. Res. Commun. 204, 468-474, 1994

```
A; Title: Role of Fas ligand in apoptosis induced by hepatitis C virus infection.
A; Reference number: JC2340; MUID: 95071350; PMID: 7980502
A; Accession: JC2340
A; Molecule type: DNA
A; Residues: 1-281 <MIT>
A; Cross-references: GB: D38122; DDBJ: D29820; NID: q601892; PIDN: BAA07320.1;
PID:q1369902
R; Schatzlein, C.E.
submitted to the EMBL Data Library, June 1995
A; Reference number: S57565
A; Accession: S57565
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-281 <SCH>
A; Cross-references: EMBL: X89102; NID: q887455; PID: q887456
R; Alderson, M.R.; Tough, T.W.; Davis-Smith, T.; Braddy, S.; Falk, B.; Schooley,
K.A.; Goodwin, R.G.; Smith, C.A.; Ramsdell, F.; Lynch, D.H.
J. Exp. Med. 181, 71-77, 1995
A; Title: Fas ligand mediates activation-induced cell death in human T
lymphocytes.
A; Reference number: 138554; MUID: 95105731; PMID: 7528780
A; Accession: I38554
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: mRNA
A; Residues: 1-281 <RE2>
A;Cross-references: EMBL:U08137; NID:q624627; PIDN:AAC50071.1; PID:q624628
C; Genetics:
A; Gene: FasL
A; Introns: 151/1; 116/3
C; Keywords: glycoprotein; transmembrane protein
F;80-102/Domain: transmembrane #status predicted <TMM>
F;76,184,250,260/Binding site: carbohydrate (Asn) (covalent) #status predicted
                        11.2%; Score 189; DB 2; Length 281;
 Query Match
 Best Local Similarity 21.7%; Pred. No. 2.2e-08;
 Matches
          69; Conservative 43; Mismatches
                                             98; Indels 108; Gaps
                                                                      11;
          22 PGAPHEGPLHAPPPPAP----HQPPAASRS------MFVALLGLGLGQVVCS 63
Qу
             : | | | | : | | | | |
Db
          46 PPPPPPPPLPPPPPPPPLPLPLPLKKRGNHSTGLCLLVMFFMVLVALVGLGLG---- 100
          64 VALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAF 123
Qy
               : 1 1
                                         1 1: :::1 :
         101 --MFQLFHLQ------ 124
Db
         124 QGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT--INATDIPSGSHK 181
Qy
               :::|:: |
                                             1: :1
         125 -SSLEKQIGH------ 159
Db
Qy
         182 VSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVY 241
                 Db
         160 ---LEWEDTYGIVLLSGVKYKKGGLVINETGLYFVYSKVYFRGQSCNN-----LPLSHK 210
         242 VTKTSIKIPSSHTLMKGGSTKY-----WSGNSEFHFYSINVGGFFKLRSGEEISIEVSN 295
Qу
             | :|| :|:| |
                                       1::1 :1 | 1 | 1 ::: 1 |
         211 VYMRNSKYPQDLVMMEGKMMSYCTTGQMWARSS-----YLGAVFNLTSADHLYVNVSE 263
Db
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Qу
         296 PSLLDPDQDATYFGAFKV 313
             ||::::::|:||:|::
Db
         264 LSLVNFEESQTFFGLYKL 281
RESULT 2
A53062
Fas ligand - mouse
C; Species: Mus musculus (house mouse)
C;Date: 06-Jan-1995 #sequence revision 06-Jan-1995 #text change 09-Jul-2004
C; Accession: A53062
R; Takahashi, T.; Tanaka, M.; Brannan, C.I.; Jenkins, N.A.; Copeland, N.G.; Suda,
T.; Nagata, S.
Cell 76, 969-976, 1994
A; Title: Generalized lymphoproliferative disease in mice, caused by a point
mutation in the Fas ligand.
A; Reference number: A53062; MUID: 94185175; PMID: 7511063
A; Accession: A53062
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-279 <TAK>
A; Cross-references: UNIPROT: P41047; GB: U06948; NID: q473564; PIDN: AAA17800.1;
PID: q473565
 Query Match
                       10.9%; Score 184.5; DB 2; Length 279;
 Best Local Similarity 21.7%; Pred. No. 5.3e-08;
          70; Conservative 45; Mismatches 106; Indels 101; Gaps
                                                                     11;
          13 RGSEEMGGGPGAPHEGPLHAPPPPAPHQP-----PAASRSMFVALLGLGL 57
Qу
                    1
                                                          : |||:|:||
          38 RGPDQRRPPPPPPPVSPLPPPSQPLPLPPLTPLKKKDHNTNLWLPVVFFMVLVALVGMGL 97
Db
          58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
Qу
                                      :|:: |
                                 -----MYQLFHL----- 105
Db
          98 G-----
         118 RIKQAFQGAVQKELQHI--VGSQHIRA---EKAMVDGSWLDLAKRSKLEAQPFAHLTINA 172
Qу
                     106 -----QKELAELREFTNQSLKVSSFEKQIANPS----TPSEKKEPRSVAHLTGN- 150
Db
         173 TDIPSGSHKVSLS-SWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDL 231
Qy
                   1 1: 1
                              1 | || : : | |::|: | |::|: : ||
         151 ----PHSRSIPLEWEDTYGTALISGVKYKKGGLVINETGLYFVYSKVYFRGQSCN--- 201
Db
         232 ATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISI 291
Qy
              202 -NQPLNHKVYMRNS--KYPEDLVLMEEKRLNYCT-TGQIWAHSSYLGAVFNLTSADHLYV 257
Db
         292 EVSNPSLLDPDQDATYFGAFKV 313
Qy
                Db
         258 NISQLSLINFEESKTFFGLYKL 279
RESULT 3
S53090
CD40 ligand - bovine
C; Species: Bos primigenius taurus (cattle)
```

```
C;Date: 08-Jul-1995 #sequence revision 21-Jul-1995 #text change 09-Jul-2004
C; Accession: S53090
R; Mertens, B.E.L.C.; Muriuki, M.
submitted to the EMBL Data Library, February 1995
A; Description: Cloning of bovine CD40L and homology to bovine TNFA and TNFB.
A; Reference number: S53090
A; Accession: S53090
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-261 <MER>
A; Cross-references: UNIPROT: P51749; EMBL: Z48469; NID: q732569; PIDN: CAA88363.1;
PID:q732570
 Query Match
                       10.5%; Score 176.5; DB 2; Length 261;
 Best Local Similarity 24.2%; Pred. No. 2.3e-07;
 Matches 70; Conservative 54; Mismatches 122; Indels
                                                          43; Gaps
                                                                     13;
          33 PPPPAPHQPPAASRSMFVALLGLGL-GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRIL 91
Qy
            8 PSPRSVATGPPVSMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE-----R 57
Db
Qу
          92 RLHENADFODT--TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDG 149
             58 NLHEDFVFMKTIQRCNKGEGSLSLLNCEEIRSRFEDLVKDIMQ----NKEVKKKEKNFE- 112
Db
         150 SWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-L 206
Qу
                     :
Db
         113 ----MHKGDQEPQIAAHVISEAS----SKTTSVLQW-APKGYYTLSNNLVTLENGKQL 161
         207 IVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIP--SSHTLMKGGSTKYW 264
Qу
             |:||||:|:|:|:|:|::::||
         162 AVKRQGFYYIYTQVTFCSNR-----ETLSQAPFIASLCLKSPSGSERILLRAANTH-- 212
Db
         265 SGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
                    Db
         213 SSSKPCGQQSIHLGGVFELQSGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
RESULT 4
A49266
fas ligand - rat
C; Species: Rattus norvegicus (Norway rat)
C;Date: 13-Jan-1995 #sequence_revision 13-Jan-1995 #text_change 09-Jul-2004
C:Accession: A49266
R; Suda, T.; Takahashi, T.; Golstein, P.; Nagata, S.
Cell 75, 1169-1178, 1993
A; Title: Molecular cloning and expression of the Fas ligand, a novel member of
the tumor necrosis factor family.
A; Reference number: A49266; MUID: 94084792; PMID: 7505205
A; Accession: A49266
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-278 <SUD>
A; Cross-references: UNIPROT: P36940; GB: U03470; NID: q440178; PIDN: AAC52129.1;
PID:q440179
C; Keywords: glycoprotein; transmembrane protein
```

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Query Match
                      10.4%; Score 175.5; DB 2; Length 278;
 Best Local Similarity 20.3%; Pred. No. 3e-07;
          64; Conservative 47; Mismatches 106; Indels 99; Gaps
          21 GPGAPHEGPLHAPPPPAPHQPPAASRSM-----FVALLGLGL 57
Qy
            111:1:11
          39 GPGQRRPPP--PPPPPSPLPPPSQPPPLPPLSPLKKKDNIELWLPVIFFMVLVALVGMGL 96
Db
          58 GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCR 117
Qу
            Db
          97 G-----MYQLFHLQKELAELREFTNHSL-RVSSFEKQIANPSTPSETKKPRSV---- 143
         118 RIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPS 177
Qy
         144 -----AHLTGNPR---- 151
Db
         178 GSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQ 237
Qv
             152 -SRSIPL-EWEDTYGTALISGVKYKKGGLVINEAGLYFVYSKVYFRGQSCN----SQPLS 205
Db
         238 LMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPS 297
Qу
              Db
         206 HKVYM--RNFKYPGDLVLMEEKKLNYCT-TGQIWAHSSYLGAVFNLTVADHLYVNISQLS 262
         298 LLDPDQDATYFGAFKV 313
Qу
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Db
         263 LINFEESKTFFGLYKL 278
RESULT 5
I53476
CD40 ligand - human
N; Alternate names: glycoprotein 39; hCD40-L protein; T-cell antigen gp39; TRAP
protein
C; Species: Homo sapiens (man)
C;Date: 02-Jul-1996 #sequence revision 02-Jul-1996 #text change 09-Jul-2004
C; Accession: S28017; JH0793; $26694; S28852; I53476; S25684; S30593
R; Hollenbaugh, D.; Grosmaire, L.S.; Kullas, C.D.; Chalupny, N.J.; Braesch-
Andersen, S.; Noelle, R.J.; Stamenkovic, I.; Ledbetter, J.A.; Aruffo, A.
EMBO J. 11, 4313-4321, 1992
A; Title: The human T cell antigen gp39, a member of the TNF gene family, is a
ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell
co-stimulatory activity.
A; Reference number: $28017; MUID: 93049181; PMID: 1385114
A; Accession: S28017
A; Molecule type: mRNA
A; Residues: 1-261 <HOL>
A; Cross-references: UNIPROT: P29965; EMBL: Z15017; NID: g38483; PIDN: CAA78737.1;
PID:g38484
R; Spriggs, M.K.; Armitage, R.J.; Strockbine, L.; Clifford, K.N.; Macduff, B.M.;
Sato, T.A.; Maliszewski, C.R.; Fanslow, W.C.
J. Exp. Med. 176, 1543-1550, 1992
A; Title: Recombinant human CD40 ligand stimulates B cell proliferation and
immunoglobulin E secretion.
A; Reference number: JH0793; MUID: 93094757; PMID: 1281209
A; Accession: JH0793
A; Molecule type: mRNA
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A; Residues: 1-261 <SPR>
A;Cross-references: GB:X67878; NID:q38411; PIDN:CAA48077.1; PID:g38412
A; Experimental source: peripheral blood T-cell
R; Graf, D.; Korthaeuer, U.; Mages, H.W.; Senger, G.; Kroczek, R.A.
Eur. J. Immunol. 22, 3191-3194, 1992
A; Title: Cloning of TRAP, a ligand for CD40 on human T cells.
A; Reference number: S26694; MUID: 93076854; PMID: 1280226
A; Accession: S26694
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-261 <GRA>
A; Cross-references: EMBL: X68550; NID: q37269; PIDN: CAA48554.1; PID: q37270
R; Gauchat, J.F.; Aubry, J.P.; Mazzei, G.; Life, P.; Jomotte, T.; Elson, G.;
Bonnefoy, J.Y.
FEBS Lett. 315, 259-266, 1993
A; Title: Human CD40-ligand: molecular cloning, cellular distribution and
regulation of expression by factors controlling IgE production.
A; Reference number: S28852; MUID: 93138085; PMID: 7678552
A; Accession: S28852
A; Molecule type: mRNA
A; Residues: 1-261 <GAU>
A;Cross-references: EMBL:L07414; NID:g180123; PIDN:AAA35662.1; PID:g180124
A; Note: the sequence from Fig. 3 is inconsistent with that from Fig. 2 in having
6-Gln
C; Genetics:
A; Gene: GDB: CD40LG; HIGM1; IMD3
A; Cross-references: GDB:120632; OMIM:308230
A; Map position: Xq26-Xq26
C; Keywords: glycoprotein; transmembrane protein
F;13-44/Domain: transmembrane #status predicted <TMM>
F;45-261/Domain: extracellular #status predicted <EXT>
F;6,240/Binding site: carbohydrate (Asn) (covalent) #status predicted
 Query Match
                         9.4%; Score 158.5; DB 2; Length 261;
 Best Local Similarity
                        24.5%; Pred. No. 7.7e-06;
           68; Conservative 53; Mismatches 113; Indels
 Matches
                                                            43; Gaps
                                                                        15;
          45 SRSMFVALLGLGL-GQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDT- 102
Qy
             111: 1 1
          20 SMKIFMYLLTVFLITQMIGSALFAVYLHRRLD--KIEDE-----RNLHEDFVFMKTI 69
Db
Qy
         103 -TLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLE 161
                 70 QRCNTGERSLSLLNCEEIKSQFEGFV-KDIM-----LNKEETKKENSF-EMQKGDQ-N 119
Db
         162 AQPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN--MTFSNGK-LIVNQDGFYYLYA 218
Qγ
              1 11: 1:
                         120 POIAAHVISEAS----SKTTSVLQW-AEKGYYTMSNNLVTLENGKQLTVKRQGLYYIYA 173
Db
         219 NICFRHHETSGDLATEYLQLMVYVTKTSIKIPS--SHTLMKGGSTKYWSGNSEFHFYSIN 276
Qу
              : | : : | :: :| | :: :|
Db
         174 QVTFCSNREASSQAP-----FIASLCLKSPGRFERILLRAANTH--SSAKPCGQQSIH 224
Qу
         277 VGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
             :|| |:|: | : : |::|| :
                                         1 11 1:
Dh
         225 LGGVFELQPGASVFVNVTDPSQVSHGTGFTSFGLLKL 261
```

RESULT 6 QWMSN tumor necrosis factor alpha precursor - mouse N; Alternate names: cachectin; TNF alpha C; Species: Mus musculus (house mouse) C;Date: 31-Mar-1988 #sequence\_revision 31-Mar-1988 #text change 09-Jul-2004 C; Accession: A22908; S03791; A27303; A25164; A23127; A34251; I59058; A36696 R; Shirai, T.; Shimizu, N.; Shiojiri, S.; Horiquchi, S.; Ito, H. DNA 7, 193-201, 1988 A; Title: Cloning and expression in Escherichia coli of the gene for mouse tumor necrosis factor. A; Reference number: A22908; MUID: 88224564; PMID: 2836146 A: Accession: A22908 A; Molecule type: DNA A; Residues: 1-235 <SHI> A; Cross-references: UNIPROT: P06804; GB: M20155 R; Shakhov, A.N.; Nedospasov, S.A. Bioorg. Khim. 13, 701-705, 1987 A; Title: Molecular cloning of the genes coding for tumor necrosis factors: complete nucleotide sequence of the genomic copy of TNF-alpha in mice. A; Reference number: S03791; MUID: 87298639; PMID: 3040015 A; Accession: S03791 A; Molecule type: DNA A; Residues: 1-235 <SHA> A; Cross-references: GB: M38296; NID: q202086; PIDN: AAA40459.1; PID: q202087 A; Note: article in Russian with English abstract R; Semon, D.; Kawashima, E.; Jongeneel, C.V.; Shakhov, A.N.; Nedospasov, S.A. Nucleic Acids Res. 15, 9083-9084, 1987 A; Title: Nucleotide sequence of the murine TNF locus, including the TNF-alpha-(tumor necrosis factor) and TNF-beta-(lymphotoxin) genes. A; Reference number: A93679; MUID: 88067722; PMID: 3684584 A; Accession: A27303 A; Molecule type: DNA A; Residues: 1-235 <SEM> A; Cross-references: GB: Y00467; NID: g54830; PIDN: CAA68530.1; PID: g54832 R; Pennica, D.; Hayflick, J.S.; Bringman, T.S.; Palladino, M.A.; Goeddel, D.V. Proc. Natl. Acad. Sci. U.S.A. 82, 6060-6064, 1985 A; Title: Cloning and expression in Escherichia coli of the cDNA for murine tumor necrosis factor. A; Reference number: A25164; MUID: 85298296; PMID: 3898078 A; Accession: A25164 A; Molecule type: mRNA A; Residues: 1-235 < PEN> A;Cross-references: GB:M11731; NID:g202084; PIDN:AAA40458.1; PID:g202085 R; Fransen, L.; Muller, R.; Marmenout, A.; Tavernier, J.; van der Heyden, J.; Kawashima, E.; Chollet, A.; Tizard, R.; van Heuverswyn, H.; van Vliet, A.; Ruysschaert, M.R.; Fiers, W. Nucleic Acids Res. 13, 4417-4429, 1985 A; Title: Molecular cloning of mouse tumour necrosis factor cDNA and its eukaryotic expression. A; Reference number: A23127; MUID: 85242112; PMID: 2989794 A; Accession: A23127 A; Molecule type: mRNA A; Residues: 1-235 <FRA> A; Cross-references: GB: X02611; NID: g54844; PIDN: CAA26457.1; PID: g54845 R;Cseh, K.; Beutler, B.

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J. Biol. Chem. 264, 16256-16260, 1989
A; Title: Alternative cleavage of the cachectin/tumor necrosis factor propeptide
results in a larger, inactive form of secreted protein.
A; Reference number: A34251; MUID: 89380231; PMID: 2777790
A; Accession: A34251
A; Molecule type: protein
A; Residues: 70-87 <CSE>
R; Caput, D.; Beutler, B.; Hartog, K.; Thayer, R.; Brown-Shimer, S.L.; Cerami, A.
Proc. Natl. Acad. Sci. U.S.A. 83, 1670-1674, 1986
A; Title: Identification of a common nucleotide sequence in the 3'-untranslated
region of mRNA molecules specifying inflammatory mediators.
A; Reference number: I59058; MUID: 86149365; PMID: 2419912
A; Accession: I59058
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: mRNA
A; Residues: 1-230, 'R', 232-235 < RES>
A; Cross-references: GB:M13049; NID:g202082; PIDN:AAA40457.1; PID:g202083
R; Sherry, B.; Jue, D.M.; Zentella, A.; Cerami, A.
Biochem. Biophys. Res. Commun. 173, 1072-1078, 1990
A; Title: Characterization of high molecular weight glycosylated forms of murine
tumor necrosis factor.
A; Reference number: A36696; MUID: 91097531; PMID: 2268312
A; Accession: A36696
A; Molecule type: protein
A; Residues: 80-85, 'X', 87-99 <SHE>
C; Genetics:
A; Introns: 62/3; 81/1; 97/1
A; Note: the first intron occurs in the 5'-untranslated region
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
F;80-235/Product: tumor necrosis factor #status experimental <MAT>
F;20/Binding site: myristate (Lys) (covalent) #status predicted
F;84/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;86/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;148-179/Disulfide bonds: #status predicted
  Query Match
                           8.4%; Score 141.5; DB 1; Length 235;
  Best Local Similarity 25.9%; Pred. No. 0.00018;
           42; Conservative 28; Mismatches
                                                  57; Indels
                                                                35; Gaps
                                                                             7;
Qy
          163 QPFAHLTINATDIPSGSHKVSLS-SWYHDRGWAKISN-MTFSNGKLIVNQDGFYYLYANI 220
              : | | | : | |
                              1:1
                                      - 1
                                          1 1 :: | | : : | : | | | | : | : :
Db
           90 KPVAHVVAN------HQVEEQLEWLSQRANALLANGMDLKDNQLVVPADGLYLVYSQV 141
          221 CFRHHETSGDLATEYLQLMVYVTK-----TSIKIPSSHTLMKGGSTKYWSGNS 268
Qу
               1:
                     1
                         :1: | |::
                                                  :::1 1
                                                              : |
                                                                   1 1
Db
          142 LFK----GQGCPDYVLLTHTVSRFAISYQEKVNLLSAVKSPCPKDTPEGAELKPW---- 192
Qу
          269 EFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
                Dh
          193 ---YEPIYLGGVFQLEKGDQLSAEVNLPKYLDFAESGQVYFG 231
```

RESULT 7 A25451

tumor necrosis factor alpha precursor - rabbit

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N; Alternate names: cachectin; TNF alpha
C; Species: Oryctolagus cuniculus (domestic rabbit)
C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 09-Jul-2004
C; Accession: A25454; A25451; JS0727
R; Ito, H.; Yamamoto, S.; Kuroda, S.; Sakamoto, H.; Kajihara, J.; Kiyota, T.;
Hayashi, H.; Kato, M.; Seko, M.
DNA 5, 149-156, 1986
A; Title: Molecular cloning and expression in Escherichia coli of the cDNA coding
for rabbit tumor necrosis factor.
A; Reference number: A25454; MUID: 86219711; PMID: 3519137
A; Accession: A25454
A; Molecule type: mRNA
A; Residues: 1-234 <ITO>
A; Cross-references: UNIPROT: P04924; GB: M12845; NID: q165759; PIDN: AAA31486.1;
PID:q165760
R; Ito, H.; Shirai, T.; Yamamoto, S.; Akira, M.; Kawahara, S.; Todd, C.W.;
Wallace, R.B.
DNA 5, 157-165, 1986
A; Title: Molecular cloning of the gene encoding rabbit tumor necrosis factor.
A; Reference number: A25451; MUID: 86219712; PMID: 3519138
A; Accession: A25451
A; Molecule type: DNA
A; Residues: 1-234 <IT2>
A; Note: this sequence differs from that shown in having a Gln inserted between
residues 62 and 63
R; Shakhov, A.N.; Kuprash, D.V.; Azizov, M.M.; Jongeneel, C.V.; Nedospasov, S.A.
Gene 95, 215-221, 1990
A; Title: Structural analysis of the rabbit TNF locus, containing the genes
encoding TNF-beta (lymphotoxin) and TNF-alpha (tumor necrosis factor).
A; Reference number: JH0309; MUID: 91065534; PMID: 2249779
A; Accession: JS0727
A; Status: nucleic acid sequence not shown; translation not shown
A; Molecule type: DNA
A; Residues: 1-62, 'Q', 63-234 <SHA>
A;Cross-references: GB:M60340; GB:M35326; NID:g165754; PIDN:AAA31484.1;
PID:g165756
C; Genetics:
A; Introns: 62/3; 80/1; 96/1
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
F;1-81/Domain: propeptide #status predicted <PRO>
F;82-234/Product: tumor necrosis factor #status predicted <MAT>
F;19,20/Binding site: myristate (Lys) (covalent) #status predicted
F;83/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;147-178/Disulfide bonds: #status predicted
  Query Match
                           8.4%; Score 141; DB 1; Length 234;
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                                  Pred. No. 0.0002;
            65; Conservative
                               35; Mismatches
                                                  99; Indels 102;
                                                                             13;
Qy
           27 EGPLHAPPPPAPHQPPAASR----SMFVALLGLGLGQVVCSVALFFYFRAQMDPNRISED 82
                                    1:1 11 1 : 1
                     - 1
                            1:1
                                                           :11
           14 EGPL----PKKAGGPQGSKRCLCLSLFSFLLVAGATTLFC----LHFRVIGPQEEESPN 65
Db
           83 GTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRA 142
Qу
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```
66 NLHLV------A 82
Db
         143 EKAMVDGSWLDLAKRSKLEAOPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISN-MTF 201
Qy
                                :| | | :: | | | :: | |
          83 SRALSD-----KPLAHVVAN----PQVEGQL---QWLSQRANALLANGMKL 121
Db
         202 SNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSHTLMKG--- 258
Qу
             122 TDNQLVVPADGLYLIYSQVLF----SGQGCRSYVLLTHTVSRFAVSYPNKVNLLSAIKS 176
         259 ----GSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYF 308
Qy
                          177 PCHRETPEEAEPMAW-----YEPIYLGGVFQLEKGDRLSTEVNQPEYLDLAESGQVYF 229
         309 G 309
Qy
         230 G 230
Db
RESULT 8
JH0529
tumor necrosis factor alpha precursor - sheep
N; Alternate names: cachectin; TNF alpha
C; Species: Ovis orientalis aries, Ovis ammon aries (domestic sheep)
C; Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 09-Jul-2004
C; Accession: JH0529; S48118; S13114; S20661
R; Green, I.R.; Sargan, D.R.
Gene 109, 203-210, 1991
A; Title: Sequence of the cDNA encoding ovine tumor necrosis factor-alpha:
problems with cloning by inverse PCR.
A; Reference number: JH0529; MUID: 92112044; PMID: 1765267
A; Accession: JH0529
A; Molecule type: mRNA
A; Residues: 1-234 <GRE>
A;Cross-references: UNIPROT:P23383; EMBL:X55152; NID:g1405; PIDN:CAA38952.1;
PID:g1406
A; Experimental source: alveolar macrophage
R; Nash, A.D.; Barcham, G.J.; Brandon, M.R.; Andrews, A.E.
Immunol. Cell Biol. 69, 273-283, 1991
A; Title: Molecular cloning, expression and characterization of ovine TNF-alpha.
A; Reference number: S48118; MUID: 92155784; PMID: 1786996
A; Accession: S48118
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-234 <NAS>
A;Cross-references: EMBL:X56756; NID:g297806; PIDN:CAA40076.1; PID:g297807
R; Young, A.J.; Hay, J.B.; Chan, J.Y.C.
Nucleic Acids Res. 18, 6723, 1990
A; Title: Primary structure of ovine tumor necrosis factor alpha cDNA.
A; Reference number: S13114; MUID: 91067496; PMID: 2251151
A; Accession: S13114
A; Status: preliminary
A; Molecule type: mRNA
A; Residues: 1-62, 64-234 <YOU>
A; Cross-references: EMBL: X55966; NID: g1403; PIDN: CAA39437.1; PID: g1404
A; Note: comparison with the introns of homologous sequences suggest that this is
probably an alternative splicing
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C; Superfamily: tumor necrosis factor
C; Keywords: alternative splicing; cytokine; cytotoxin; qlycoprotein;
lipoprotein; lymphokine; macrophage; myristylation; transmembrane protein
F;1-77/Domain: propeptide #status predicted <PRO>
F;78-234/Product: tumor necrosis factor alpha #status predicted <TUM>
F;20/Binding site: myristate (Lys) (covalent) #status predicted
F;82/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;96/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;146-178/Disulfide bonds: #status predicted
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                         26.1%; Pred. No. 0.00043;
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                              30; Mismatches
                                                71; Indels
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          134 IVGSQHIRAEKAMVDGSW---LDLAKRSKLEA---QPFAHLTINATDIPSGSHKVSLSSW 187
Qу
              ::| | | |::
                             1:
                                  - 1
                                       || :|
                                                :| ||: |
           55 VIGPQ--REEQSPAGPSFNRPLVQTLRSSSQASNNKPVAHVVAN-----ISAP 100
Db
          188 YHDRGWAKISNMTFSNG-----KLIVNQDGFYYLYANICFRHH-----ETSGDL 231
Qу
                      : | : | |
                                    :|:| || || :|: : || |
Db
          101 GQLRWGDSYANALMANGVELKDNQLVVPTDGLYLIYSQVLFRGHGCPSTPLFLTHTISRI 160
         232 ATEYLOLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISI 291
Qу
              1 | 1 | : ::|| |
                                     ::|
                                          1 1
                                                 : | || |:| |: :|
          161 AVSY-QTKVNIL-SAIKSPCHRETLEGAEAKPW-----YEPIYQGGVFQLEKGDRLSA 211
Db
         292 EVSNPSLLD-PDQDATYFG 309
Qу
              1:: | || :
          212 EINLPEYLDYAESGQVYFG 230
Db
RESULT 9
QWHUN
tumor necrosis factor alpha precursor [validated] - human
N; Alternate names: cachectin; TNFA
C; Species: Homo sapiens (man)
C;Date: 28-Aug-1985 #sequence revision 28-Aug-1985 #text change 09-Jul-2004
C; Accession: A93585; S36153; A93351; A44189; B61478; I53311; S62610; I54522;
A01646; B23784
R; Nedwin, G.E.; Naylor, S.L.; Sakaguchi, A.Y.; Smith, D.; Jarrett-Nedwin, J.;
Pennica, D.; Goeddel, D.V.; Gray, P.W.
Nucleic Acids Res. 13, 6361-6373, 1985
A; Title: Human lymphotoxin and tumor necrosis factor genes: structure, homology
and chromosomal localization.
A; Reference number: A93585; MUID: 86016093; PMID: 2995927
A; Accession: A93585
A; Molecule type: DNA
A; Residues: 1-233 <NED>
A; Cross-references: UNIPROT: P01375; GB: X02910; GB: X02159; NID: q37209;
PIDN:CAA26669.1; PID:q37210
R; Iris, F.J.M.; Bouqueleret, L.; Prieur, S.; Caterina, D.; Primas, G.; Perrot,
V.; Jurka, J.; Rodriguez-Tome, P.; Claverie, J.M.; Dausset, J.; Cohen, D.
Nature Genet. 3, 137-145, 1993
A; Title: Dense Alu clustering and a potential new member of the NFkappaB family
within a 90 kilobase HLA class III segment.
A; Reference number: S36152; MUID: 93272029; PMID: 8499947
A; Accession: S36153
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A; Status: nucleic acid sequence not shown; translation not shown
A; Molecule type: DNA
A; Residues: 1-233 <IRI>
A; Cross-references: EMBL: Z15026; NID: q37211; PIDN: CAA78745.1; PID: q37212
A; Note: the nucleotide sequence was submitted to the EMBL Data Library, August
1992
R; Pennica, D.; Nedwin, G.E.; Hayflick, J.S.; Seeburg, P.H.; Derynck, R.;
Palladino, M.A.; Kohr, W.J.; Aggarwal, B.B.; Goeddel, D.V.
Nature 312, 724-729, 1984
A; Title: Human tumour necrosis factor: precursor structure, expression and
homology to lymphotoxin.
A; Reference number: A93351; MUID: 85086244; PMID: 6392892
A; Accession: A93351
A; Molecule type: mRNA
A; Residues: 1-233 < PEN>
A; Cross-references: GB: X02910; GB: X02159; NID: q37209; PIDN: CAA26669.1;
PID:q37210
A; Note: this protein was isolated from the monocyte-like cell line HL-60 from a
promyelocytic leukemia
R; Wang, A.M.; Creasey, A.A.; Ladner, M.B.; Lin, L.S.; Strickler, J.; Van
Arsdell, J.N.; Yamamoto, R.; Mark, D.F.
Science 228, 149-154, 1985
A; Title: Molecular cloning of the complementary DNA for human tumor necrosis
factor.
A; Reference number: A44189; MUID: 85142190; PMID: 3856324
A; Accession: A44189
A; Molecule type: mRNA
A; Residues: 1-62, 'S', 64-233 <WAN>
A; Cross-references: GB: M10988; NID: q339737; PIDN: AAA61198.1; PID: q339738
R; Fukuda, S.; Ando, S.; Sanou, O.; Taniai, M.; Fujii, M.; Masaki, N.; Nakamura,
K.I.; Ando, O.; Torigoe, K.; Sugimoto, T.; Kurimoto, M.
Lymphokine Res. 7, 175-185, 1988
A; Title: Simultaneous production of natural human tumor necrosis factor-alpha, -
beta and interferon-alpha from BALL-1 cells stimulated by HVJ.
A; Reference number: A61478; MUID: 88301617; PMID: 2841543
A; Accession: B61478
A; Molecule type: protein
A; Residues: 83-102; 109-119; 121-128, 'X', 130-131; 142-144, 'X', 146, 'XXX', 150-
152;159-174;180,'X',182-204 <FUK>
R; Marmenout, A.; Fransen, L.; Tavernier, J.; Van Der Heyden, J.; Tizard, R.;
Kawashima, E.; Shaw, A.; Johnson, M.
Eur. J. Biochem. 152, 515-522, 1985
A; Title: Molecular cloning and expression of human tumor necrosis factor and
comparison with mouse tumor nectosis factor.
A; Reference number: I53311; MUID: 86030296; PMID: 3932069
A; Accession: I53311
A; Status: translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-233 <MAR>
A;Cross-references: GB:M26331; NID:q339763; PIDN:AAA36758.1; PID:q339764
A; Experimental source: U-937 cells
R; Takakura-Yamamoto, R.; Yamamoto, S.; Fukuda, S.; Kurimoto, M.
Eur. J. Biochem. 235, 431-437, 1996
A; Title: O-Glycosylated species of natural human tumor-necrosis factor-alpha.
A; Reference number: S62610; MUID: 96202967; PMID: 8631363
A; Accession: S62610
```

A; Molecule type: protein

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R; D'Alfonso, S.; Richiardi, P.M.
Immunogenetics 39, 150-154, 1994
A; Title: A polymorphic variation in a putative regulation box of the TNFA
promoter region.
A; Reference number: I54522; MUID: 94102809; PMID: 7903959
A; Accession: I54522
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-8 < DAL>
A; Cross-references: GB:S68530; NID:g544751
R; Stevenson, F.T.; Bursten, S.L.; Locksley, R.M.; Lovett, D.H.
J. Exp. Med. 176, 1053-1062, 1992
A; Title: Myristyl acylation of the tumor necrosis factor alpha precursor on
specific lysine residues.
A; Reference number: A59163; MUID: 93018820; PMID: 1402651
A; Contents: annotation; identification of myristylated lysines
R; Aggarwal, B.B.; Kohr, W.J.; Hass, P.E.; Moffat, B.; Spencer, S.A.; Henzel,
W.J.; Bringman, T.S.; Nedwin, G.E.; Goeddel, D.V.; Harkins, R.N.
J. Biol. Chem. 260, 2345-2354, 1985
A; Title: Human tumor necrosis factor. Production, purification, and
characterization.
A; Reference number: A92511; MUID: 85130974; PMID: 3871770
A; Contents: annotation; disulfide bond
C; Comment: Secreted from mitogen-activated macrophages within 4-24 hours after
induction, TNF-alpha can cause cytolysis of certain tumor cell lines and have an
antiproliferative effect on others without detriment to normal cells. It can
also act synergistically with interferon gamma to kill certain transformed cell
lines.
C; Comment: TNF-alpha and -beta (lymphotoxin) are the products of different genes
closely linked on chromosome 6. They are induced by similar mitogenic stimuli
and have similar biological activities but are produced by different cell types
and have different induction kinetics.
C; Genetics:
A; Gene: GDB: TNF; TNFA
A; Cross-references: GDB:120441; OMIM:191160
A; Map position: 6p21.3-6p21.3
A; Introns: 62/3; 78/1; 94/1
C; Complex: homotrimer
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; homotrimer; lipoprotein;
lymphokine; macrophage; membrane protein; myristylation
F;1-76/Domain: propeptide #status predicted <PRO>
F;77-233/Product: tumor necrosis factor #status experimental <MAT>
F;19,20/Binding site: myristate (Lys) (covalent) #status experimental
F;81/Binding site: carbohydrate (Ser) (covalent) (partial) #status experimental
F;145-177/Disulfide bonds: #status experimental
  Query Match
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              :1-11:-1
                          ::
                                      | : | | ::| : : :|:| :| | :|: :
           87 KPVAHVVAN----PQAEGQL---QWLNRRANALLANGVELRDNQLVVPSEGLYLIYSQVL 139
Db
          222 FRHH--ETSGDLATEYLQLMV--YVTK----TSIKIPSSHTLMKGGSTKYWSGNSEFHFY 273
Qy
```

A; Residues: 77-99 <TAK>

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          140 FKGQGCPSTHVLLTHTISRIAVSYQTKVNLLSAIKSPCQRETPEGAEAKPW-----YE 192
Db
         274 SINVGGFFKLRSGEEISIEVSNPSLLD-PDQDATYFG 309
Qу
              1:11 1:1 1: 1 1: 1 1 :
Db
         193 PIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFG 229
RESULT 10
I54490
tumor necrosis factor alpha precursor - white-footed mouse
C; Species: Peromyscus leucopus (white-footed mouse)
C;Date: 02-Aug-1996 #sequence revision 02-Aug-1996 #text change 09-Jul-2004
C; Accession: I54490
R; Crew, M.D.; Filipowsky, M.E.
Immunogenetics 35, 351-353, 1992
A; Title: Sequence of the tumor necrosis factor/cachectin (TNF) gene from
Peromyscus leucopus (family Cricetidae).
A; Reference number: I54490; MUID: 92218012; PMID: 1348497
A; Accession: I54490
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-235 < RES>
A; Cross-references: UNIPROT: P36939; GB: M59233; NID: q202506; PIDN: AAA40596.1;
PID: g202507
C; Genetics:
A; Gene: PlTNF
A; Introns: 62/3; 81/1; 97/1
C; Superfamily: tumor necrosis factor
C; Keywords: glycoprotein; lipoprotein; myristylation
F;19,20/Binding site: myristate (Lys) (covalent) #status predicted
F;84/Binding site: carbohydrate (Ser) (covalent) #status predicted
 Query Match
                          7.9%; Score 132.5; DB 2; Length 235;
 Best Local Similarity 25.3%; Pred. No. 0.0011;
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           42; Conservative 27; Mismatches 54; Indels
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Qу
         163 QPFAHLTINATDIPSGSHKVSLSSWYHDRGWAKISNMTFSNG-----KLIVNQDGFYYL 216
                             1:1 : 11
                                             :1 :11
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          90 KPVAHVVAN------HQVDEQLEWLSRG----ANALLANGMDLKDNQLVIPADGLYLV 137
         217 YANICFRHHETSGDLATEYLOLMVYVTK-----TSIKIPSSHTLMKGGSTKYW 264
Qv
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             1: : 1:
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Db
         138 YSQVLFK-----GQGCSSYVLLTHTVSRFAVSYEDKVNLLSAIKSPCPKETPEGSELKPW 192
         265 SGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD-PDODATYFG 309
Qу
                 Πh
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tumor necrosis factor alpha precursor - rat
N; Alternate names: cachectin; TNF alpha
C; Species: Rattus norvegicus (Norway rat)
C;Date: 07-Jun-1990 #sequence revision 07-Jun-1990 #text change 09-Jul-2004
C; Accession: JU0029; JN0868; S21674
```

```
R; Shirai, T.; Shimizu, N.; Horiguchi, S.; Ito, H.
Agric. Biol. Chem. 53, 1733-1736, 1989
A; Title: Cloning and expression in Escherichia coli of the gene for rat tumor
necrosis factor.
A; Reference number: JU0029
A:Accession: JU0029
A; Molecule type: DNA
A; Residues: 1-235 <SHI>
A; Cross-references: UNIPROT: P16599
R; Kwon, J.; Chung, I.Y.; Benveniste, E.N.
Gene 132, 227-236, 1993
A:Title: Cloning and sequence analysis of the rat tumor necrosis factor-encoding
genes.
A; Reference number: JN0868; MUID: 94040766; PMID: 8224868
A; Accession: JN0868
A; Molecule type: DNA
A; Residues: 1-235 <KWO>
A;Cross-references: GB:L00981; NID:q205253; PIDN:AAA16275.1; PID:g205254
R; Estler, H.C.; Grewe, M.; Gaussling, R.; Pavlovic, M.; Decker, K.
Biol. Chem. Hoppe-Seyler 373, 271-281, 1992
A; Title: Rat tumor necrosis factor-alpha. Transcription in rat Kupffer cells and
in vitro posttranslational processing based on a PCR-derived cDNA.
A; Reference number: S21674; MUID: 92329007; PMID: 1627266
A; Accession: S21674
A; Molecule type: mRNA
A; Residues: 1-38, 'P', 40-162, 'T', 164-201, 'S', 203-235 <EST>
A;Cross-references: GB:X66539; GB:S40199; NID:g395369; PIDN:CAA47146.1;
PID:q395370
C; Comment: Tumor necrosis factor is secreted by macrophages in response to
endotoxin and produces hemorrhagic necrosis of tumors.
C; Genetics:
A; Gene: TNF-alpha
A; Introns: 62/3; 81/1; 97/1
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; glycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
F;80-235/Product: tumor necrosis factor #status predicted <MAT>
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F;84/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;86/Binding site: carbohydrate (Asn) (covalent) #status predicted
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C;Date: 02-Jul-1996 #sequence revision 02-Jul-1996 #text change 09-Jul-2004
C; Accession: I49139; I49138; I49076
R; Lawton, P.; Nelson, J.; Tizard, R.; Browning, J.L.
J. Immunol. 154, 239-246, 1995
A; Title: Characterization of the mouse lymphotoxin-beta gene.
A; Reference number: I49138; MUID: 95088371; PMID: 7995944
A; Accession: I49139
A; Status: translated from GB/EMBL/DDBJ
A; Molecule type: mRNA
A; Residues: 1-306 < RES>
A;Cross-references: UNIPROT:P41155; EMBL:U16985; NID:g577830; PIDN:AAA70089.1;
PID:q577831
A; Accession: I49138
A; Status: translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-306 < RE3>
A;Cross-references: EMBL:U16984; NID:g577431; PIDN:AAB60493.1; PID:g577432
R; Pokholok, D.K.; Maroulakou, I.G.; Kuprash, D.V.; Alimzhanov, M.B.; Kozlov,
S.V.; Novobrantseva, T.I.; Turetskaya, R.L.; Green, J.E.; Nedospasov, S.A.
Proc. Natl. Acad. Sci. U.S.A. 92, 674-678, 1995
A; Title: Cloning and expression analysis of the murine lymphotoxin beta gene.
A; Reference number: A55602; MUID: 95148600; PMID: 7846035
A; Accession: I49076
A; Status: preliminary
A; Molecule type: DNA
A; Residues: 1-306 < RE2>
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A; Gene: LT-beta
A; Introns: 54/3; 160/1
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C; Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 09-Jul-2004
C; Accession: S22052
R; Sanjanwala, M.; Edwards, A.
submitted to the EMBL Data Library, September 1991
A; Description: Baboon Tumor Necrosis Factor Derived from Sequences of Genomic
DNA.
A; Reference number: S22052
A; Accession: S22052
A; Status: preliminary
A; Molecule type: DNA
A; Residues: 1-233 <SAN>
A;Cross-references: UNIPROT:P33620; EMBL:X62141; NID:g38159; PIDN:CAA44068.1;
PID:q38160
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A; Introns: 62/3; 78/1; 94/1
C; Superfamily: tumor necrosis factor
C; Keywords: glycoprotein; lipoprotein; myristylation; transmembrane protein
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F;81/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;145-177/Disulfide bonds: #status predicted
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N; Alternate names: cachectin; TNF alpha
C; Species: Equus caballus (domestic horse)
C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 09-Jul-2004
C; Accession: JQ1344
R;Su, X.; Morris, D.D.; McGraw, R.A.
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Gene 107, 319-321, 1991

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necrosis factor alpha.
A; Reference number: JQ1344; MUID: 92084125; PMID: 1748301
A; Accession: JQ1344
A; Molecule type: DNA
A; Residues: 1-234 <SUX>
A; Cross-references: UNIPROT: P29553; GB: M64087; NID: q164244; PIDN: AAA30959.1;
PID:g164245
C; Comment: This protein is an important proximal mediator of endotoxemia.
C; Genetics:
A; Gene: TNF-alpha
A; Introns: 62/3; 79/1; 95/1
C; Superfamily: tumor necrosis factor
C; Keywords: cytokine; cytotoxin; qlycoprotein; lipoprotein; lymphokine;
macrophage; membrane protein; myristylation
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C; Species: Bos primigenius taurus (cattle)
C;Date: 10-Sep-1999 #sequence revision 10-Sep-1999 #text change 09-Jul-2004
C; Accession: I46047; S24642
R; Cludts, I.; Cleuter, Y.; Kettmann, R.; Burny, A.; Droogmans, L.
Cytokine 5, 336-341, 1993
A; Title: Cloning and characterization of the tandemly arranged bovine
lymphotoxin and tumour necrosis factor-alpha genes.
A; Reference number: I46046; MUID: 94083525; PMID: 8260599
A; Accession: I46047
A; Status: preliminary; translated from GB/EMBL/DDBJ
A; Molecule type: DNA
A; Residues: 1-233 <CL2>
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PID:g798
C; Genetics:
A; Gene: TNFA
A; Introns: 62/3; 78/1; 94/1
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A; Title: Cloning and characterization of gene TNF alpha encoding equine tumor

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C; Superfamily: tumor necrosis factor
C; Keywords: glycoprotein; lipoprotein; myristylation; transmembrane protein
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F;145-177/Disulfide bonds: #status predicted
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Job time : 42 secs

# GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: November 8, 2004, 18:29:02; Search time 170 Seconds

(without alignments)

658.662 Million cell updates/sec

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Post-processing: Minimum Match 0%

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Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

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2	1685	100.0	317	9	US-09-871-856-13	Sequence 13, Appl
. 3	1685	100.0	317	9	US-09-957-944-6	Sequence 6, Appli
4	1685	100.0	317	9	US-09-865-363-13	Sequence 13, Appl
5	1685	100.0	317	9	US-09-871-291-13	Sequence 13, Appl
6	1685	100.0	317	9	US-09-877-650-13	Sequence 13, Appl
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45	1293	76.7	245	13	US-10-017-910-2	Sequence 2, Appli

## ALIGNMENTS

RESULT 1 US-09-813-329-7

<sup>;</sup> Sequence 7, Application US/09813329
; Patent No. US20020012968A1

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; GENERAL INFORMATION:
  APPLICANT: Bristol-Myers Suibb Company
  TITLE OF INVENTION: No. US20020012968Alel Drosophila Tumor Necrosis Factor
Class Molecule ("DmTNF") and
  TITLE OF INVENTION: Variants Thereof
  FILE REFERENCE: D0016.np
  CURRENT APPLICATION NUMBER: US/09/813,329
  CURRENT FILING DATE: 2001-03-20
  PRIOR APPLICATION NUMBER: 60/190,816
  PRIOR FILING DATE: 2000-03-21
  NUMBER OF SEQ ID NOS: 65
  SOFTWARE: PatentIn version 3.0
 SEO ID NO 7
   LENGTH: 317
   TYPE: PRT
   ORGANISM: Drosophila melanogaster
US-09-813-329-7
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RESULT 2
US-09-871-856-13
; Sequence 13, Application US/09871856
 Patent No. US20020081720A1
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
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```
CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/871,856
            FILING DATE: 31-May-2001
            CLASSIFICATION: <Unknown>
       PRIOR APPLICATION DATA:
            APPLICATION NUMBER: 08/996,139
            FILING DATE: <Unknown>
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
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; Sequence 6, Application US/09957944
; Publication No. US20020086312A1
; GENERAL INFORMATION:
  APPLICANT: Dougall, William C.
  TITLE OF INVENTION: SCREENING ASSAYS FOR AGONISTS AND ANTAGONISTS OF RECEPTOR
ACTIVATOR OF
  TITLE OF INVENTION: NF-kappa B
  FILE REFERENCE: 3109-A
  CURRENT APPLICATION NUMBER: US/09/957,944
  CURRENT FILING DATE: 2001-09-20
  PRIOR APPLICATION NUMBER: 60/235,157
  PRIOR FILING DATE: 2000-09-22
  NUMBER OF SEQ ID NOS: 13
  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 6
   LENGTH: 317
   TYPE: PRT
   ORGANISM: Homo sapiens
US-09-957-944-6
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; Sequence 13, Application US/09865363
; Publication No. US20020086826A1
    GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
                    Galibert, Laurent
                    Maraskovsky, Eugene
         TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
         NUMBER OF SEQUENCES: 19
         CORRESPONDENCE ADDRESS:
             ADDRESSEE: Immunex Corporation, Law Department
              STREET: 51 University Street
              CITY: Seattle
              STATE: WA
              COUNTRY: USA
              ZIP: 98101
         COMPUTER READABLE FORM:
             MEDIUM TYPE: Floppy disk
              COMPUTER: Apple Power Macintosh
              OPERATING SYSTEM: Apple Operating System 7.5.5
              SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
         CURRENT APPLICATION DATA:
              APPLICATION NUMBER: US/09/865,363
              FILING DATE: 25-May-2001
              CLASSIFICATION: <Unknown>
         PRIOR APPLICATION DATA:
              APPLICATION NUMBER: 08/995,659
              FILING DATE: <Unknown>
              APPLICATION NUMBER: USSN 08/813,509
              FILING DATE: 07 MARCH 1997
              APPLICATION NUMBER: USSN 08/772,330
              FILING DATE: 23 DECEMBER 1996
         ATTORNEY/AGENT INFORMATION:
              NAME: Perkins, Patricia Anne
              REGISTRATION NUMBER: 34,693
              REFERENCE/DOCKET NUMBER: 2852-A
         TELECOMMUNICATION INFORMATION:
              TELEPHONE: (206) 587-0430
              TELEFAX: (206)233-0644
    INFORMATION FOR SEQ ID NO: 13:
         SEQUENCE CHARACTERISTICS:
              LENGTH: 317 amino acids
              TYPE: amino acid
              TOPOLOGY: linear
         MOLECULE TYPE: protein
         SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-865-363-13
                          100.0%; Score 1685; DB 9; Length 317;
  Query Match
                          100.0%; Pred. No. 2.5e-149;
  Best Local Similarity
  Matches 317; Conservative
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US-09-871-291-13
; Sequence 13, Application US/09871291
; Publication No. US20020086827A1
  GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
       CORRESPONDENCE ADDRESS:
           ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
           CITY: Seattle
           STATE: WA
           COUNTRY: USA
           ZIP: 98101
       COMPUTER READABLE FORM:
           MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
           OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
           APPLICATION NUMBER: US/09/871,291
            FILING DATE: 30-May-2001
           CLASSIFICATION: <Unknown>
       PRIOR APPLICATION DATA:
           APPLICATION NUMBER: 08/996,139
            FILING DATE: <Unknown>
           APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
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APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
           NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2851-A
       TELECOMMUNICATION INFORMATION:
           TELEPHONE: (206) 587-0430
           TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
           TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-871-291-13
 Query Match
                      100.0%; Score 1685; DB 9; Length 317;
 Best Local Similarity
                      100.0%; Pred. No. 2.5e-149;
 Matches 317; Conservative
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US-09-877-650-13
; Sequence 13, Application US/09877650
; Patent No. US20020169117A1
   GENERAL INFORMATION:
       APPLICANT: Anderson, Dirk M.
                 Galibert, Laurent
                 Maraskovsky, Eugene
       TITLE OF INVENTION: Ligand for Receptor Activator of NF-kappaB
       NUMBER OF SEQUENCES: 19
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CORRESPONDENCE ADDRESS:
            ADDRESSEE: Immunex Corporation, Law Department
            STREET: 51 University Street
            CITY: Seattle
            STATE: WA
            COUNTRY: USA
            ZIP: 98101
       COMPUTER READABLE FORM:
            MEDIUM TYPE: Floppy disk
            COMPUTER: Apple Power Macintosh
            OPERATING SYSTEM: Apple Operating System 7.5.5
            SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
       CURRENT APPLICATION DATA:
            APPLICATION NUMBER: US/09/877,650
            FILING DATE: 08-Jun-2001
            CLASSIFICATION: <Unknown>
       PRIOR APPLICATION DATA:
            APPLICATION NUMBER: 08/995,659
            FILING DATE: 1997-12-22
            APPLICATION NUMBER: USSN 08/813,509
            FILING DATE: 07 MARCH 1997
            APPLICATION NUMBER: USSN 08/772,330
            FILING DATE: 23 DECEMBER 1996
       ATTORNEY/AGENT INFORMATION:
            NAME: Perkins, Patricia Anne
            REGISTRATION NUMBER: 34,693
            REFERENCE/DOCKET NUMBER: 2852-A
       TELECOMMUNICATION INFORMATION:
            TELEPHONE: (206) 587-0430
            TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
       SEQUENCE CHARACTERISTICS:
            LENGTH: 317 amino acids
            TYPE: amino acid
            TOPOLOGY: linear
       MOLECULE TYPE: protein
       SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-09-877-650-13
 Query Match
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RESULT 7
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; Sequence 10, Application US/10151071
; Publication No. US20030017151A1
; GENERAL INFORMATION:
  APPLICANT: DOUGALL, William
  APPLICANT: ANDERSON, Dirk
  TITLE OF INVENTION: THERAPEUTIC USES OF RANK ANTAGONISTS
  FILE REFERENCE: 3277-A
  CURRENT APPLICATION NUMBER: US/10/151,071
  CURRENT FILING DATE: 2001-05-17
  PRIOR APPLICATION NUMBER: 60/291,919
  PRIOR FILING DATE: 2001-05-17
  NUMBER OF SEQ ID NOS: 10
  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 10
   LENGTH: 317
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   ORGANISM: Homo sapiens
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Db

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RESULT 8
US-10-218-547-22
; Sequence 22, Application US/10218547
; Publication No. US20030100074A1
; GENERAL INFORMATION:
  APPLICANT: Human Genome Sciences, Inc.
  TITLE OF INVENTION: Methods And Compositions For Treating Metabolic Bone
Diseases Relating To
  TITLE OF INVENTION: Human Endokine Alpha
  FILE REFERENCE: PF561
  CURRENT APPLICATION NUMBER: US/10/218,547
  CURRENT FILING DATE: 2002-08-15
  PRIOR APPLICATION NUMBER: 60/312,542
  PRIOR FILING DATE: 2001-08-16
  PRIOR APPLICATION NUMBER: 60/330,761
  PRIOR FILING DATE: 2001-10-30
  NUMBER OF SEQ ID NOS: 57
  SOFTWARE: PatentIn version 3.1
 SEO ID NO 22
   LENGTH: 317
   TYPE: PRT
   ORGANISM: human
US-10-218-547-22
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RESULT 9
US-10-405-878-13
; Sequence 13, Application US/10405878
 Publication No. US20030175840A1
   GENERAL INFORMATION:
        APPLICANT: Anderson, Dirk M.
;
                   Galibert, Laurent
                   Maraskovsky, Eugene
        TITLE OF INVENTION: Receptor Activator of NF-kappaB
        NUMBER OF SEQUENCES: 19
        CORRESPONDENCE ADDRESS:
             ADDRESSEE: Immunex Corporation, Law Department
             STREET: 51 University Street
             CITY: Seattle
             STATE: WA
             COUNTRY: USA
             ZIP: 98101
        COMPUTER READABLE FORM:
             MEDIUM TYPE: Floppy disk
             COMPUTER: Apple Power Macintosh
             OPERATING SYSTEM: Apple Operating System 7.5.5
             SOFTWARE: Microsoft Word for Power Macintosh 6.0.1
        CURRENT APPLICATION DATA:
             APPLICATION NUMBER: US/10/405,878
             FILING DATE: 01-Apr-2003
             CLASSIFICATION: <Unknown>
        PRIOR APPLICATION DATA:
             APPLICATION NUMBER: US/08/996,139
             FILING DATE: 22 DECEMBER 1997
             APPLICATION NUMBER: USSN 60/064,671
             FILING DATE: 14 OCTOBER 1997
             APPLICATION NUMBER: USSN 08/813,509
             FILING DATE: 07 MARCH 1997
             APPLICATION NUMBER: USSN 08/772,330
             FILING DATE: 23 DECEMBER 1996
        ATTORNEY/AGENT INFORMATION:
             NAME: Perkins, Patricia Anne
             REGISTRATION NUMBER: 34,693
             REFERENCE/DOCKET NUMBER: 2851-A
        TELECOMMUNICATION INFORMATION:
             TELEPHONE: (206) 587-0430
             TELEFAX: (206)233-0644
   INFORMATION FOR SEQ ID NO: 13:
        SEQUENCE CHARACTERISTICS:
             LENGTH: 317 amino acids
             TYPE: amino acid
             TOPOLOGY: linear
        MOLECULE TYPE: protein
        SEQUENCE DESCRIPTION: SEQ ID NO: 13:
US-10-405-878-13
                         100.0%; Score 1685; DB 14; Length 317;
 Query Match
 Best Local Similarity 100.0%; Pred. No. 2.5e-149;
 Matches 317; Conservative 0; Mismatches 0; Indels 0; Gaps
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## RESULT 10

US-10-167-182-11

- ; Sequence 11, Application US/10167182
- ; Publication No. US20030176647A1
- ; GENERAL INFORMATION:
- ; APPLICANT: Yamaquchi, Kyoji
- ; APPLICANT: Yasuda, Hisataka
- ; APPLICANT: Nakagawa, No. US20030176647Aluaki
- ; APPLICANT: Shima, No. US20030176647A1uyuki
- ; APPLICANT: Kinosaki, Masahiko
- ; APPLICANT: Tsuda, Eisuke
- ; APPLICANT: Goto, Masaaki
- ; APPLICANT: Yano, Kazuki
- ; APPLICANT: Tomoyasu, Akihiro
- ; APPLICANT: Kobayashi, Fumie
- ; APPLICANT: Washida, Naohiro
- ; APPLICANT: Takahashi, Ken
- ; APPLICANT: Morinaga, Tomonori
- ; APPLICANT: Higashio, Kanji
- ; TITLE OF INVENTION: Antibodies to OCIF-binding Molecules
- ; FILE REFERENCE: FJN-070DV
- ; CURRENT APPLICATION NUMBER: US/10/167,182
- ; CURRENT FILING DATE: 2002-06-11
- ; PRIOR APPLICATION NUMBER: US 09/202,455
- ; PRIOR FILING DATE: 1998-12-15
- ; PRIOR APPLICATION NUMBER: JP 97808/1997
- ; PRIOR FILING DATE: 1997-04-15
- ; PRIOR APPLICATION NUMBER: JP 151434/1997
- ; PRIOR FILING DATE: 1997-06-09
- ; PRIOR APPLICATION NUMBER: JP 217897/1997
- ; PRIOR FILING DATE: 1997-08-12
- ; PRIOR APPLICATION NUMBER: JP 224803/1997
- ; PRIOR FILING DATE: 1997-08-21
- ; PRIOR APPLICATION NUMBER: JP 332241/1997

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PRIOR FILING DATE: 1997-12-02
  PRIOR APPLICATION NUMBER: WO PCT/JP98/01728
  PRIOR FILING DATE: 1998-04-15
  NUMBER OF SEQ ID NOS: 19
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RESULT 11
US-10-310-793-28
; Sequence 28, Application US/10310793
; Publication No. US20030198640A1
; GENERAL INFORMATION:
 APPLICANT: Yu, Guo-Liang
  APPLICANT: Ni, Jian
  APPLICANT: Rosen, Craig A
  APPLICANT:
            Zhang, Jun
  APPLICANT:
            Wei, Ping
  TITLE OF INVENTION: Methods And Compositions For Treating Inflammatory Bowel
  TITLE OF INVENTION:
                    Relating To Human Tumor Necrosis Factor-Gamma Beta
  FILE REFERENCE: PF573
  CURRENT APPLICATION NUMBER: US/10/310,793
  CURRENT FILING DATE: 2002-12-06
  PRIOR APPLICATION NUMBER: 60/336,695
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PRIOR FILING DATE: 2001-12-07
  PRIOR APPLICATION NUMBER: 10/226,294
  PRIOR FILING DATE: 2002-08-23
  PRIOR APPLICATION NUMBER: 60/314,381
  PRIOR FILING DATE: 2001-08-24
  PRIOR APPLICATION NUMBER: 09/899,059
  PRIOR FILING DATE: 2001-07-06
 PRIOR APPLICATION NUMBER: 60/278,449
  PRIOR FILING DATE: 2001-03-26
  PRIOR APPLICATION NUMBER: 60/216,879
  PRIOR FILING DATE: 2000-07-07
  PRIOR APPLICATION NUMBER: 09/559,290
  PRIOR FILING DATE: 2000-04-27
  PRIOR APPLICATION NUMBER: 60/180,908
  PRIOR FILING DATE: 2000-02-08
  PRIOR APPLICATION NUMBER: 60/134,067
  PRIOR FILING DATE: 1999-05-13
  PRIOR APPLICATION NUMBER: 60/132,227
  PRIOR FILING DATE: 1999-05-03
  Remaining Prior Application data removed - See File Wrapper or PALM.
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; Sequence 11, Application US/10460623
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 GENERAL INFORMATION:
  APPLICANT: Yamaguchi, Kyoji
             Yasuda, Hisataka
  APPLICANT:
             Nakagawa, No. US20030208045Aluaki
  APPLICANT:
  APPLICANT:
              Shima, No. US20030208045Aluyuki
             Kinosaki, Masahiko
  APPLICANT:
  APPLICANT:
             Tsuda, Eisuke
              Goto, Masaaki
  APPLICANT:
  APPLICANT:
              Yano, Kazuki
  APPLICANT:
              Tomoyasu, Akihiro
              Kobayashi, Fumie
  APPLICANT:
              Washida, Naohiro
  APPLICANT:
  APPLICANT:
              Takahashi, Ken
  APPLICANT: Morinaga, Tomonori
             Higashio, Kanji
  APPLICANT:
  TITLE OF INVENTION: No. US20030208045Alel Protein and Method for Producing
the Protein
  FILE REFERENCE: FJN-070
  CURRENT APPLICATION NUMBER: US/10/460,623
  CURRENT FILING DATE: 2003-06-13
  PRIOR APPLICATION NUMBER: JP 97808/1997
  PRIOR FILING DATE: 1997-04-15
  PRIOR APPLICATION NUMBER: JP 151434/1997
  PRIOR FILING DATE: 1997-06-09
  PRIOR APPLICATION NUMBER: JP 217897/1997
  PRIOR FILING DATE: 1997-08-12
  PRIOR APPLICATION NUMBER: JP 224803/1997
  PRIOR FILING DATE: 1997-08-21
  PRIOR APPLICATION NUMBER: JP 332241/1997
  PRIOR FILING DATE: 1997-12-02
  PRIOR APPLICATION NUMBER: WO PCT/JP98/01728
  PRIOR FILING DATE: 1998-04-15
  NUMBER OF SEQ ID NOS: 19
  SOFTWARE: PatentIn Ver. 2.0
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   LENGTH: 317
   TYPE: PRT
   ORGANISM: Homo sapiens
US-10-460-623-11
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                                 Pred. No. 2.5e-149;
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RESULT 13
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; Sequence 79, Application US/10289456
; Publication No. US20040033211A1
; GENERAL INFORMATION:
  APPLICANT: Bachmann, Martin
  APPLICANT: Maurer, Patrick
  APPLICANT: Spohn, Gunther
  TITLE OF INVENTION: Antigen Arrays for Treatment of Bone Disease
  FILE REFERENCE: 1700.0330001
  CURRENT APPLICATION NUMBER: US/10/289,456
  CURRENT FILING DATE: 2002-11-07
  PRIOR APPLICATION NUMBER: PCT/IB02/00166
  PRIOR FILING DATE: 2002-01-21
  PRIOR APPLICATION NUMBER: US 10/050,902
  PRIOR FILING DATE: 2002-01-18
  PRIOR APPLICATION NUMBER: US 60/396,635
  PRIOR FILING DATE: 2002-07-19
  PRIOR APPLICATION NUMBER: US 60/331,045
  PRIOR FILING DATE: 2001-11-07
  NUMBER OF SEQ ID NOS: 170
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 SEO ID NO 79
   LENGTH: 317
   TYPE: PRT
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; Sequence 22, Application US/10202062
 Publication No. US20040038349A1
 GENERAL INFORMATION:
  APPLICANT: Human Genome Sciences, Inc.,
  TITLE OF INVENTION: Heteromultimeric TNF Ligand Family members
  FILE REFERENCE: PF559
  CURRENT APPLICATION NUMBER: US/10/202,062
  CURRENT FILING DATE: 2002-07-25
  PRIOR APPLICATION NUMBER: 60/307,838
  PRIOR FILING DATE: 2001-07-27
  NUMBER OF SEQ ID NOS: 42
  SOFTWARE: PatentIn version 3.0
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; Sequence 2, Application US/10664801
 Publication No. US20040115199A1
 GENERAL INFORMATION:
  APPLICANT: M&E Biotech A/S
  APPLICANT: HALKIER, Torben
  APPLICANT: HAANING, Jesper
  TITLE OF INVENTION: Method for Down-Regulating Osteoprotegerin Ligand
  TITLE OF INVENTION: Activity
  FILE REFERENCE: 22021 PC 1
  CURRENT APPLICATION NUMBER: US/10/664,801
  CURRENT FILING DATE: 2003-09-17
  PRIOR APPLICATION NUMBER: US/09/396,937
  PRIOR FILING DATE: 1999-09-15
  NUMBER OF SEQ ID NOS: 35
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Search completed: November 8, 2004, 18:44:23

Job time: 173 secs

## GenCore version 5.1.6 Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: November 8, 2004, 18:23:14; Search time 192 Seconds

(without alignments)

949.968 Million cell updates/sec

Title: US-09-787-126-2

Perfect score: 1685

Sequence: 1 MRRASRDYTKYLRGSEEMGG.....LLDPDQDATYFGAFKVRDID 317

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 1825181 seqs, 575374646 residues

Total number of hits satisfying chosen parameters: 1825181

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database: UniProt\_02:\*

1: uniprot\_sprot:\*
2: uniprot\_trembl:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

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4	1292	76.7	244	2	BAB79693	Bab79693 homo sapi
5	266	15.8	317	2	Q7ZYX9	Q7zyx9 brachydanio
6	265	15.7	304	2	Q7T1F2	Q7t1f2 gallus gall
7	251.5	14.9	281	1	TN10 HUMAN	P50591 homo sapien
8	251.5	14.9	281	2	CAG33176	Cag33176 homo sapi
9	249.5	14.8	299	2	Q6DHG9	Q6dhg9 brachydanio
10	248	14.7	291	1	TN10 MOUSE	P50592 mus musculu
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12	216.5	12.8	287	2	Q90WT9 `	Q90wt9 gallus gall
13	215.5	12.8	287	2	Q8K3G0	Q8k3g0 rattus norv
14	200	11.9	282	1	TNF6_PIG	Q9bea8 sus scrofa
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16	189	11.2	281	1	TNF6 HUMAN	P48023 homo sapien
17	189	11.2	281	2	AA043991	Aao43991 homo sapi
18	187.5	11.1	279	2	Q7TMV9	Q7tmv9 mus musculu
19	186	11.0	280	1	TNF6 MACMU	Q9myl6 macaca mula
20	184.5	10.9	252	2	Q8K3 <u>Y</u> 8	Q8k3y8 mus musculu
21	184.5	10.9	279	1	TNF6 MOUSE	P41047 mus musculu
22	184.5	10.9	279	2	BAC30520	Bac30520 mus muscu
23	182.5	10.8	280	1	TNF6 CERTO	Q9bdn1 cercocebus
24	181	10.7	95	2	Q6UWL7	Q6uwl7 homo sapien
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27	181	10.7	95	2	AAQ89101	Aaq89101 homo sapi
28	179.5	10.7	252	2	Q80YZ0	Q80yz0 mus musculu
29	177.5	10.5	252	2	Q8K3Y7	Q8k3y7 rattus norv
30	176.5	10.5	261	1	TNF5_BOVIN	P51749 bos taurus
31	175.5	10.4	278	1	TNF6_RAT	P36940 rattus norv
32	169.5	10.1	261	1	TNF5_CALJA	Q9bdn3 callithrix
33	167.5	9.9	261	1	TNF5_AOTTR	Q9bdm3 aotus trivi
34	158.5	9.4	261	1	TNF5_HUMAN	P29965 homo sapien
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36	156.5	9.3	251	2	Q8NFE9	Q8nfe9 homo sapien
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38	155.5	9.2	261	1	TNF5_MACMU	Q9bdc7 macaca mula
39	155	9.2	272	1	TNF5_CHICK	Q9i8d8 gallus gall
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41	152	9.0	260	1	TNF5_FELCA	097605 felis silve
42	146	8.7	234	1	TNFA_CAVPO	P51435 cavia porce
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44	145	8.6	174	1	TN15_HUMAN	095150 homo sapien
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## ALIGNMENTS

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     16-OCT-2001 (Rel. 40, Last sequence update)
DT
DT
     05-JUL-2004 (Rel. 44, Last annotation update)
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DE
     induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast
DE
     differentiation factor) (ODF).
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     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
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     Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
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     TISSUE=Bone marrow, and Peripheral blood;
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     Anderson D.M., Maraskovsky E., Billingsley W.L., Dougall W.C.,
RA
     Tometsko M.E., Roux E.R., Teepe M.C., DuBose R.F., Cosman D.,
RA
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Galibert L.;
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     "A homologue of the TNF receptor and its ligand enhance T-cell growth
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     and dendritic-cell function.";
     Nature 390:175-179(1997).
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     "Osteoprotegerin ligand is a cytokine that regulates osteoclast
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     Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
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RP
RC
     TISSUE=Thymocytes;
RX
     MEDLINE=97460112; PubMed=9312132;
RA
     Wong B.R., Rho J., Arron J., Robinson E., Orlinick J., Chao M.,
     Kalachikov S., Cayani E., Bartlett F.S. III, Frankel W.N., Lee S.Y.,
RA
RA
     Choi Y.;
RT
     "TRANCE is a novel ligand of the tumor necrosis factor receptor family
RT
    that activates c-Jun N-terminal kinase in T cells.";
     J. Biol. Chem. 272:25190-25194(1997).
RL
RN
     [5]
     SEQUENCE FROM N.A. (ISOFORM 2).
RP
RC
     TISSUE=Tonque;
     MEDLINE=20175237; PubMed=10708588; DOI=10.1006/bbrc.2000.2314;
RX
     Nagai M., Kyakumoto S., Sato N.;
RA
     "Cancer cells responsible for humoral hypercalcemia express mRNA
RT
     encoding a secreted form of ODF/TRANCE that induces osteoclast
RT
     formation.";
RT
     Biochem. Biophys. Res. Commun. 269:532-536(2000).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF11B/OPG and to
CC
         TNFRSF11A/RANK. Osteoclast differentiation and activation factor.
CC
         Augments the ability of dendritic cells to stimulate naive T-cell
CC
         proliferation. May be an important regulator of interactions
CC
         between T cells and dendritic cells and may play a role in the
CC
         regulation of the T cell-dependent immune response. May also play
CC
         an important role in enhanced bone-resorption in humoral
CC
CC
         hypercalcemia of malignancy.
CC
     -!- SUBUNIT: Homotrimer (By similarity).
     -!- SUBCELLULAR LOCATION: Type II membrane protein (isoforms 1 and 3);
CC
         Secreted (isoform 2). A soluble form of isoform 1 arises by
CC
         proteolytic processing (By similarity).
CC
     -!- ALTERNATIVE PRODUCTS:
CC
         Event=Alternative splicing; Named isoforms=3;
CC
CC
         Name=1;
           IsoId=014788-1; Sequence=Displayed;
CC
         Name=2; Synonyms=SODF;
CC
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CC
          IsoId=014788-2; Sequence=VSP 006447;
CC
        Name=3:
CC
          IsoId=014788-3; Sequence=VSP 006446;
CC
     -!- TISSUE SPECIFICITY: Highest in the peripheral lymph nodes, weak in
CC
        spleen, peripheral blood Leukocytes, bone marrow, heart, placenta,
CC
        skeletal muscle, stomach and thyroid.
CC
     -!- INDUCTION: Up-regulated by T cell receptor stimulation.
CC
     -!- PTM: The soluble form of isoform 1 derives from the membrane form
CC
        by proteolytic processing (By similarity). The cleavage may be
        catalyzed by ADAM17.
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     _____
CC
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    between the Swiss Institute of Bioinformatics and the EMBL outstation -
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     the European Bioinformatics Institute. There are no restrictions on its
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    use by non-profit institutions as long as its content is in no way
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    modified and this statement is not removed. Usage by and for commercial
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     entities requires a license agreement (See http://www.isb-sib.ch/announce/
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    or send an email to license@isb-sib.ch).
CC
     .
CC
     EMBL; AF019047; AAB86811.1; -.
DR
    EMBL; AF053712; AAC39731.1; -.
DR
     EMBL; AB064269; BAB79694.1; -.
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    EMBL; AB061227; BAB71768.1; -.
DR
    EMBL; AB064270; BAB79695.1; -.
DR
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DR
     EMBL; AB037599; BAA90488.1; -.
    HSSP; 035235; 1JTZ.
DR
DR
    Genew; HGNC:11926; TNFSF11.
DR
    MIM; 602642; -.
     GO; GO:0005576; C:extracellular; NAS.
DR
     GO; GO:0005887; C:integral to plasma membrane; NAS.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; NAS.
DR
    GO; GO:0006955; P:immune response; NAS.
DR
     GO; GO:0030316; P:osteoclast differentiation; NAS.
DR
     InterPro; IPR006052; TNF family.
DR
     InterPro; IPR008983; TNF like.
DR
     InterPro; IPR003636; TNF subf.
DR
     Pfam; PF00229; TNF; 1.
DR
     ProDom; PD002012; TNF subf; 1.
DR
     SMART; SM00207; TNF; \overline{1}.
DR
     PROSITE; PS00251; TNF 1; FALSE NEG.
DR
     PROSITE; PS50049; TNF 2; 1.
DR
    Alternative splicing; Cytokine; Differentiation; Glycoprotein;
KW
     Receptor; Signal-anchor; Transmembrane.
KW
                                 Tumor necrosis factor ligand superfamily
                       317
FT
    CHAIN
                  1
                                 member 11, membrane form.
FT
                                 Tumor necrosis factor ligand superfamily
     CHAIN
                140
                       317
FT
                                 member 11, soluble form (By similarity).
FT
                                 Cytoplasmic (Potential).
                        47
FT
     DOMAIN
                  1
                                 Signal-anchor for type II membrane
FT
     TRANSMEM
                 48
                        68
                                 protein (Potential).
FT
FT
     DOMAIN
                 69
                       317
                                 Extracellular (Potential).
                       140
                                 Cleavage (By similarity).
FT
     SITE
                139
                171
                       171
                                 N-linked (GlcNAc. . .) (Potential).
FT
     CARBOHYD
                                 N-linked (GlcNAc. . .) (Potential).
FΤ
                198
                       198
     CARBOHYD
                                 Missing (in isoform 3).
                        47
FT
     VARSPLIC
                  1
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/FTId=VSP 006446.
FT
                1
                      73
                              Missing (in isoform 2).
FT
    VARSPLIC
                              /FTId=VSP 006447.
FT
FT
    CONFLICT
               194
                     194
                              A \rightarrow G (in Ref. 4).
    SEQUENCE
              317 AA;
                      35478 MW; 766176446348097F CRC64;
SQ
 Query Match
                       100.0%; Score 1685; DB 1; Length 317;
 Best Local Similarity
                       100.0%; Pred. No. 1.2e-134;
         317; Conservative
                             0; Mismatches
                                             0; Indels
                                                          0; Gaps
 Matches
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGLGQV 60
Qу
            1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLGQV 60
Db
          61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Qу
            61 VCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIK 120
Db
         121 OAFOGAVOKELOHIVGSOHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Qу
            121 OAFOGAVOKELOHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSH 180
Db
         181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Qу
            181 KVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMV 240
Db
         241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Qу
            241 YVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLD 300
Db
         301 PDODATYFGAFKVRDID 317
Qу
            11111111111111111
         301 PDQDATYFGAFKVRDID 317
Db
RESULT 2
TN11 MOUSE
                  STANDARD;
                               PRT:
                                     316 AA.
    TN11 MOUSE
TD
    035235; 035306; Q9JJK8; Q9JJK9; Q9R1Y0;
AC
    16-OCT-2001 (Rel. 40, Created)
DT
    16-OCT-2001 (Rel. 40, Last sequence update)
DT
    01-OCT-2004 (Rel. 45, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 11 (Receptor activator
DE
    of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-
DE
    induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast
DE
    differentiation factor) (ODF) (Osteoclastogenesis-inhibitory factor)
DE
DE
     (OCIF).
    Name=Tnfsf11; Synonyms=RANKL, Trance, OPGL;
GN
    Mus musculus (Mouse).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OC
    NCBI TaxID=10090;
OX
RN
     [1]
    SEQUENCE FROM N.A. (ISOFORM 1).
RP
RC
    TISSUE=Hybridoma;
    MEDLINE=97460112; PubMed=9312132;
RX
    Wong B.R., Rho J., Arron J., Robinson E., Orlinick J., Chao M.,
RA
```

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Kalachikov S., Cayani E., Bartlett F.S. III, Frankel W.N., Lee S.Y.,
RA
RA
    Choi Y.;
     "TRANCE is a novel ligand of the tumor necrosis factor receptor family
RT
     that activates c-Jun N-terminal kinase in T cells.";
RT
     J. Biol. Chem. 272:25190-25194(1997).
RL
RN
     [2]
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
    TISSUE=Thymic lymphoma;
RC
    MEDLINE=98032977; PubMed=9367155;
RX
     Anderson D.M., Maraskovsky E., Billingsley W.L., Dougall W.C.,
RA
     Tometsko M.E., Roux E.R., Teepe M.C., DuBose R.F., Cosman D.,
RA
     Galibert L.;
RA
     "A homologue of the TNF receptor and its ligand enhance T-cell growth
RT
     and dendritic-cell function.";
RT
     Nature 390:175-179(1997).
RL
RN
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
     TISSUE=Bone marrow;
RC
     MEDLINE=98227661; PubMed=9568710;
RX
     Lacey D.L., Timms E., Tan H.-L., Kelley M.J., Dunstan C.R.,
RA
     Burgess T., Elliott R., Colombero A., Elliott G., Scully S., Hsu H.,
RA
     Sullivan J., Hawkins N., Davy E., Capparelli C., Eli A., Qian Y.-X.,
RA
     Kaufman S., Sarosi I., Shalhoub V., Senaldi G., Guo J., Delaney J.,
RA
RA
     Boyle W.J.;
     "Osteoprotegerin ligand is a cytokine that regulates osteoclast
RT
     differentiation and activation.";
RT
     Cell 93:165-176(1998).
RL
RN
     [4]
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
RC
     TISSUE=Bone marrow stroma;
RX
     MEDLINE=98188248; PubMed=9520411;
     Yasuda H., Shima N., Nakagawa N., Yamaguchi K., Kinosaki M.,
RA
     Mochizuki S.-I., Tomoyasu A., Yano K., Goto M., Murakami A., Tsuda E.,
RA.
     Morinaga T., Higashio K., Udagawa N., Takahashi N., Suda T.;
RA
     "Osteoclast differentiation factor is a ligand for
RT
     osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical
RT
     to TRANCE/RANKL.";
RT
     Proc. Natl. Acad. Sci. U.S.A. 95:3597-3602(1998).
RL
RN
     [5]
     SEQUENCE FROM N.A. (ISOFORM 1).
RP
RC
     STRAIN=129;
     MEDLINE=99214075; PubMed=10196481; DOI=10.1016/S0378-1119(99)00025-6;
RX
     Kodaira K., Kodaira K., Mizuno A., Yasuda H., Shima N., Murakami A.,
RA
     Ueda M., Higashio K.;
RA
     "Cloning and characterization of the gene encoding mouse osteoclast
RT
     differentiation factor.";
RT
RL
     Gene 230:121-127(1999).
RN
     SEQUENCE FROM N.A. (ISOFORMS 1; 2 AND 3).
RP
     MEDLINE=21150053; PubMed=11250921;
RX
     Ikeda T., Kasai M., Utsuyama M., Hirokawa K.;
RA
     "Determination of three isoforms of the receptor activator of nuclear
RT
     factor-kappaB ligand and their differential expression in bone and
RΤ
RT
     thymus.";
     Endocrinology 142:1419-1426(2001).
RL
RN
     SEQUENCE OF 139-147, PROCESSING, AND N-GLYCOSYLATION.
RP
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RX
    MEDLINE=99240759; PubMed=10224132;
    Lum L., Wong B.R., Josien R., Becherer J.D., Erdjument-Bromage H.,
RA
RA
     Schloendorff J., Tempst P., Choi Y., Blobel C.P.;
     "Evidence for a role of a tumor necrosis factor-alpha (TNF-alpha)-
RT
     converting enzyme-like protease in shedding of TRANCE, a TNF family
RT
    member involved in osteoclastogenesis and dendritic cell survival.";
RT
RL
     J. Biol. Chem. 274:13613-13618(1999).
RN
     [8]
    X-RAY CRYSTALLOGRAPHY (2.6 ANGSTROMS) OF 158-316.
RP
    MEDLINE=21464816; PubMed=11581298;
RX
     Lam J., Nelson C.A., Ross F.P., Teitelbaum S.L., Fremont D.H.;
RA
     "Crystal structure of the TRANCE/RANKL cytokine reveals determinants
RT
     of receptor-ligand specificity.";
RT
     J. Clin. Invest. 108:971-979(2001).
RL
RN
     [9]
    X-RAY CRYSTALLOGRAPHY (2.2 ANGSTROMS) OF 137-316.
RP
    MEDLINE=21839021; PubMed=11733492; DOI=10.1074/jbc.M106525200;
RX
     Ito S., Wakabayashi K., Ubukata O., Hayashi S., Okada F., Hata T.;
RA
     "Crystal structure of the extracellular domain of mouse RANK ligand at
RT
     2.2-A resolution.";
RT
     J. Biol. Chem. 277:6631-6636(2002).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF11B/OPG and to
CC
         TNFRSF11A/RANK. Osteoclast differentiation and activation factor.
CC
CC
         Augments the ability of dendritic cells to stimulate naive T-cell
         proliferation. May be an important regulator of interactions
CC
         between T cells and dendritic cells and may play a role in the
CC
         regulation of the T cell-dependent immune response. May also play
CC
CC
         an important role in enhanced bone-resorption in humoral
CC
         hypercalcemia of malignancy.
CC
     -!- SUBUNIT: Homotrimer.
     -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted
CC
         (isoforms 1 and 2); Cytoplasmic (isoform 3).
CC
CC
     -!- ALTERNATIVE PRODUCTS:
         Event=Alternative splicing; Named isoforms=3;
CC
CC
         Name=1;
           IsoId=035235-1; Sequence=Displayed;
CC
CC
         Name=2;
CC
           IsoId=035235-2; Sequence=VSP_006449;
CC
           IsoId=O35235-3; Sequence=VSP 006448;
CC
     -!- TISSUE SPECIFICITY: Highly expressed in thymus and lymph nodes,
CC
         but not in nonlymphoid tissues and is abundantly expressed in T
CC
         cells but not in B cells. A high level expression is also seen in
CC
CC
         the trabecular bone and lung.
CC
     -!- PTM: N-glycosylated.
     -!- PTM: The soluble form of isoform 1 derives from the membrane form
CC
         by proteolytic processing. The cleavage may be catalyzed by
CC
         ADAM17. A further shorter soluble form was observed.
CC
     -!- DISEASE: Deficiency in Tnfsfl1 results in failure to form lobulo-
CC
         alveolar mammary structures during pregnancy, resulting in death
CC
         of newborns. Trance-deficient mice show severe osteopetrosis, with
CC
         no osteoclasts, marrow spaces, or tooth eruption, and exhibit
CC
         profound growth retardation at several skeletal sites, including
CC
         the limbs, skull, and vertebrae and have marked chondrodysplasia,
CC
         with thick, irregular growth plates and a relative increase in
CC
CC
         hypertrophic chondrocytes.
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
```

```
CC
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     or send an email to license@isb-sib.ch).
CC
CC
     EMBL; AF013170; AAC71061.1; -.
DR
     EMBL; AF019048; AAB86812.1; -.
DR
     EMBL; AF053713; AAC40113.1; -.
DR
     EMBL; AB008426; BAA25425.1; -.
DR
     EMBL; AB022039; BAA36970.1; -.
DR
     EMBL; AB022036; BAA36970.1; JOINED.
DR
     EMBL; AB022037; BAA36970.1; JOINED.
DR
     EMBL; AB022038; BAA36970.1; JOINED.
DR
     EMBL; AB032771; BAA97257.1; -.
DR
     EMBL; AB032772; BAA97258.1; -.
DR
     EMBL; AB036798; BAA97259.1;
DR
     PDB; 1IQA; X-ray; A/B/C=157-316.
DR
DR
     PDB; 1JTZ; X-ray; X/Y/Z=146-316.
     MGD; MGI:1100089; Tnfsf11.
DR
     GO; GO:0005515; F:protein binding; IPI.
DR
     GO; GO:0042804; F:protein homooligomerization activity; IDA.
DR
DR
     GO; GO:0045453; P:bone resorption; IDA.
DR
     GO; GO:0009887; P:organogenesis; IMP.
DR
     GO; GO:0001503; P:ossification; IMP.
     GO; GO:0045670; P:regulation of osteoclast differentiation; IDA.
DR
DR
     InterPro; IPR006052; TNF_family.
     InterPro; IPR008983; TNF_like.
DR
DR
     InterPro; IPR003636; TNF_subf.
DR
     Pfam; PF00229; TNF; 1.
DR
     ProDom; PD002012; TNF subf; 1.
DR
     SMART; SM00207; TNF; 1.
     PROSITE; PS00251; TNF 1; FALSE NEG.
DR
     PROSITE; PS50049; TNF 2; 1.
DR
     3D-structure; Alternative splicing; Cytokine; Differentiation;
KW
     Direct protein sequencing; Glycoprotein; Receptor; Signal-anchor;
KW
KW
     Transmembrane.
                                   Tumor necrosis factor ligand superfamily
                         316
FT
     CHAIN
                                   member 11, membrane form.
FT
                                   Tumor necrosis factor ligand superfamily
                         316
FT
     CHAIN
                 139
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FT
                          48
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FT
     DOMAIN
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                          69
FT
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                  49
                                   protein (Potential).
FT
FT
                  70
                         316
                                   Extracellular (Potential).
     DOMAIN
                         139
FT
     SITE
                  138
                                   Cleavage.
                                   N-linked (GlcNAc. . .) (Potential).
FT
     CARBOHYD
                  197
                         197
                                   N-linked (GlcNAc. . .) (Potential).
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                          44
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FT
                                   G \rightarrow D (in Ref. 2).
                   99
                          99
FT
     CONFLICT
```

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Missing (in Ref. 5).
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               164
                     169
FΤ
    STRAND
    TURN
               171
                     172
FT
    STRAND
               181
                     182
FT
               186
                     187
    STRAND
FT
               191
                     192
FT
    TURN
               194
                     196
FT
    STRAND
    STRAND
               198
                     201
FT
                     203
               202
    TURN
FT
                       84.1%; Score 1417.5; DB 1; Length 316;
 Query Match
                       84.3%; Pred. No. 6.1e-112;
 Best Local Similarity
                                                                    2;
 Matches 268; Conservative 16; Mismatches
                                            31:
                                                Indels
                                                         3;
                                                             Gaps
          1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLH-APPPPAPHQPPAASRSMFVALLGLGLGQ 59
Qy
            1 MRRASRDYGKYLRSSEEMGSGPGVPHEGPLHPAPSAPAPAPPPAASRSMFLALLGLGLGQ 60
Db
         60 VVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRI 119
Qy
            61 VVCSIALFLYFRAQMDPNRISEDSTHCFYRILRLHENAGLQDSTLESEDT--LPDSCRRM 118
Db
         120 KQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGS 179
Qу
            111111111111111
                                  119 KQAFQGAVQKELQHIVGPQRFSGAPAMMEGSWLDVAQRGKPEAQPFAHLTINAASIPSGS 178
Db
         180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
Qу
            179 HKVTLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPTDYLQLM 238
Db
         240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
Qу
            239 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISIQVSNPSLL 298
Db
         300 DPDODATYFGAFKVRDID 317
Qу
            111111111111111111
         299 DPDQDATYFGAFKVQDID 316
Db
RESULT 3
TN11 RAT
                  STANDARD;
                               PRT:
                                     318 AA.
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ID
    Q9ESE2; Q91ZI9;
AC
    28-FEB-2003 (Rel. 41, Created)
DT
    28-FEB-2003 (Rel. 41, Last sequence update)
DT
    05-JUL-2004 (Rel. 44, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 11 (Receptor activator
    of nuclear factor kappa B ligand) (RANKL) (TNF-related activation-
DE
    induced cytokine) (TRANCE) (Osteoprotegerin ligand) (OPGL) (Osteoclast
DE
    differentiation factor) (ODF).
DΕ
    Name=Tnfsf11; Synonyms=RANKL, Trance, Opgl;
    Rattus norvegicus (Rat).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OC
OX
    NCBI TaxID=10116;
RN
    [1]
    SEQUENCE FROM N.A.
RP
```

141

143

```
RC
    TISSUE=Tibial bone;
    MEDLINE=20540945; PubMed=11092398;
RX
    Xu J.K., Tan J.K., Huang L., Gao X.H., Laird R., Liu D., Wysocki S.,
RA
RA
    Zheng M.H.;
     "Cloning, sequence and functional characterization of the rat
RT
    homologue of receptor activator of NF-kB ligand.";
RT
    J. Bone Miner. Res. 15:2178-2186(2000).
RL
RN
    [2]
    SEQUENCE OF 266-318 FROM N.A.
RP
    STRAIN=Fischer 344;
RC
    MEDLINE=21662371; PubMed=11804028;
RX
    Odgren P.R., Kim N., van Wesenbeeck L., MacKay C., Mason-Savas A.,
RA
    Safadi F.F., Popoff S.N., Lengner C., van-Hul W., Choi Y.,
RA
    Marks S.C. Jr.;
RA
     "Evidence that the rat osteopetrotic mutation toothless (tl) is not in
RT
    the TNFSF11 (TRANCE, RANKL, ODF, OPGL) gene.";
RT
    Int. J. Dev. Biol. 45:853-859(2001).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF11B/OPG and to
CC
        TNFRSF11A/RANK. Osteoclast differentiation and activation factor.
CC
        Augments the ability of dendritic cells to stimulate naive T-cell
CC
         proliferation. May be an important regulator of interactions
CC
         between T cells and dendritic cells and may play a role in the
CC
         regulation of the T cell-dependent immune response. May also play
CC
         an important role in enhanced bone-resorption in humoral
CC
CC
         hypercalcemia of malignancy.
CC
     -!- SUBUNIT: Homotrimer (By similarity).
     -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
CC
         similarity).
CC
     -!- TISSUE SPECIFICITY: Highly expressed in thymus and bone tissues.
     -!- PTM: The soluble form derives from the membrane form by
CC
CC
         proteolytic processing (By similarity).
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     _____
CC
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CC
     between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC
     the European Bioinformatics Institute. There are no restrictions on its
CC
     use by non-profit institutions as long as its content is in no way
CC
     modified and this statement is not removed. Usage by and for commercial
CC
     entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC
     or send an email to license@isb-sib.ch).
CC
     ______
CC
     EMBL; AF187319; AAG17031.1; -.
DR
DR
     EMBL; AF425669; AAL23963.1; -.
     HSSP; 035235; 1JTZ.
DR
     RGD; 620784; Tnfsf11.
DR
     InterPro; IPR006052; TNF family.
DR
     InterPro; IPR008983; TNF like.
DR
     InterPro; IPR003636; TNF subf.
DR
     Pfam; PF00229; TNF; 1.
DR
DR
     ProDom; PD002012; TNF subf; 1.
DR
     SMART; SM00207; TNF; 1.
     PROSITE; PS00251; TNF 1; FALSE NEG.
DR
     PROSITE; PS50049; TNF 2; 1.
DR
     Cytokine; Differentiation; Glycoprotein; Receptor; Signal-anchor;
KW
KW
     Transmembrane.
                                 Tumor necrosis factor ligand superfamily
                        318
FT
     CHAIN
                                 member 11, membrane form.
\mathbf{FT}
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Tumor necrosis factor ligand superfamily
FΤ
    CHAIN
               141
                     318
                              member 11, soluble form.
FT
FT
    DOMAIN
                 1
                      47
                              Cytoplasmic (Potential).
                              Signal-anchor for type II membrane
FT
    TRANSMEM
                48
                      68
                              protein (Potential).
FT
    DOMAIN
                69
                     318
                              Extracellular (Potential).
FT
    SITE
               140
                     141
                              Cleavage (By similarity).
FT
    CARBOHYD
               199
                     199
                              N-linked (GlcNAc. . .) (Potential).
FT
               264
                     264
                              N-linked (GlcNAc. . .) (Potential).
    CARBOHYD
FT
                     317
                              I \rightarrow M \text{ (in Ref. 2)}.
FT
    CONFLICT
               317
              318 AA;
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SO
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                       82.9%; Score 1396.5; DB 1; Length 318;
 Query Match
                       82.4%; Pred. No. 3.8e-110;
 Best Local Similarity
 Matches 262; Conservative 19; Mismatches
                                             36;
                                                 Indels
                                                           1;
                                                              Gaps
                                                                      1;
           1 MRRASRDYTKYLRGSEEMGGGPGAPHEGPLH-APPPPAPHQPPAASRSMFVALLGLGLGQ 59
Qy
            1 MRRANRDYGKYLRGSEEMGSCPGVPHEGPLHPAPSAPAPAPPPAASRFMFLALLGLGLGQ 60
Db
          60 VVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRI 119
Qy
            61 VVCSIALFLYFRAQMDPNRISEDSTRCFYRILRLRENTGLQDSTLESEDTEALPDSCRRM 120
Db
         120 KQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGS 179
Qy
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                                   121 KOAFOGAVORELQHIVGPQRFSGVPAMMEGSWLDVARRGKPEAQPFAHLTINAADIPSGS 180
Db
         180 HKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLM 239
QУ
            181 HKVSLSSWYHDRGWAKISNMTLSNGKLRVNQDGFYYLYANICFRHHETSGSVPADYLQLM 240
Db
         240 VYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLL 299
Qу
            241 VYVVKTSIKIPSSHNLMKGGSTKNWSGNSEFHFYSINVGGFFKLRAGEEISVQVSNPSLL 300
Db
         300 DPDQDATYFGAFKVRDID 317
Qу
            1111111111111111
         301 DPDQDATYFGAFKVQDID 318
Db
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                                      244 AA.
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               PRELIMINARY;
                                PRT;
ID
    BAB79693;
AC
    24-MAR-2004 (TrEMBLrel. 27, Created)
DT
    24-MAR-2004 (TrEMBLrel. 27, Last sequence update)
DT
    24-MAR-2004 (TrEMBLrel. 27, Last annotation update)
DT
    Receptor activator of nuclear factor kappa B ligand 3.
DΕ
    HRANKL 3.
GN
os
    Homo sapiens (Human).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OC
    NCBI TaxID=9606;
OX
RN
    [1]
RΡ
    SEQUENCE FROM N.A.
    Suzuki J., Ikeda T., Kuroyama H., Seki S., Kasai M., Utsuyama M.,
RA
```

```
Tatsumi M., Uematsu H., Hirokawa K.;
RA
RT
    "Regulation of osteoclastogenesis by three human RANKL isoforms
    expressed in NIH3T3 cells.";
RT
RL
    Biochem. Biophys. Res. Commun. 314:1021-1027(2004).
DR
    EMBL; AB064268; BAB79693.1; -.
KW
    Receptor.
                      27690 MW; C827590684B6B83C CRC64;
SQ
    SEQUENCE
              244 AA;
                       76.7%; Score 1292; DB 2; Length 244;
 Query Match
                       100.0%; Pred. No. 2e-101;
 Best Local Similarity
 Matches 244; Conservative
                              0; Mismatches
                                                 Indels
                                                                      0;
          74 MDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQH 133
Qy
             1 MDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQH 60
Db
         134 IVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGW 193
Qy
             61 IVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDRGW 120
Db
         194 AKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSH 253
Qу
             121 AKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSH 180
Db
         254 TLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
QУ
             181 TLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 240
Db
         314 RDID 317
Qу
             1111
Db
         241 RDID 244
RESULT 5
Q7ZYX9
               PRELIMINARY;
                                PRT;
                                      317 AA.
ID
    Q7ZYX9
AC
    Q7ZYX9;
DT
    01-JUN-2003 (TrEMBLrel. 24, Created)
    01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DE
    Tnfsf101 protein.
    Name=tnfsf101;
GN
    Brachydanio rerio (Zebrafish) (Danio rerio).
os
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Actinoptervgii; Neoptervgii; Teleostei; Ostariophysi; Cypriniformes;
OC
    Cyprinidae; Danio.
oc
    NCBI TaxID=7955;
OX
RN
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RP
    STRAIN=AB; TISSUE=Whole body;
RC
    MEDLINE=22388257; PubMed=12477932;
RX
     Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA
    Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA
    Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA
     Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA
     Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA
     Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA
```

```
RA
    Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA
    Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA
    Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
    Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA
    Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA
RA
    Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
    Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA
RA
    Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA
    Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M., Butterfield Y.S.,
    Krzywinski M.I., Skalska U., Smailus D.E., Schnerch A., Schein J.E.,
RA
    Jones S.J., Marra M.A.;
RA
RT
    "Generation and initial analysis of more than 15,000 full-length human
RT
    and mouse cDNA sequences.";
    Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RL
RN
    [2]
RP
    SEQUENCE FROM N.A.
RC
    STRAIN=AB; TISSUE=Whole body;
    Strausberg R.;
RA
    Submitted (JAN-2003) to the EMBL/GenBank/DDBJ databases.
RL
DR
    EMBL; BC044336; AAH44336.1; -.
DR
    HSSP; P50591; 1D2Q.
DR
    ZFIN; ZDB-GENE-010801-1; tnfsf101.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
               317 AA; 35465 MW;
                                  68F76BC1A40DCE9F CRC64;
SQ
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                        15.8%; Score 266; DB 2; Length 317;
  Query Match
  Best Local Similarity
                        26.6%; Pred. No. 4.1e-14;
                              66; Mismatches 122; Indels
           79; Conservative
          42 PAASR----SMFVALLGLGLG-QVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRL 93
Qу
                        :::|:: : : |: : || | | ::: |
             \Pi = \Pi
                                                                 I I I
          24 PANSRGRDSPSKLWIAMVVIVVVLQIASTTGLFVYL--NMSLSQVKSQGVTEELRCLGL 81
Db
          94 HENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLD 153
Qу
                           :| :|:::::|
                                                  |: |: |:
          82 -LNVLGKDQDIPEDLAQLFGEPCMKLAEGIKAYISKVTDSIISKQTLHAARTRTHSYNTT 140
Db
         154 LAK-RSKLEAQPFAHLTINATDIPS-----GSHKVSLSSWYHDRGWAKISN 198
Qу
                                                  1::::::
              141 GSKFMTTVMQRPSAHLTLSSASDNSRPQSDMHQPQFDLHQSCRHPVHTWANKSFGAHLYN 200
Db
         199 MTFSNGKLIVNQDGFYYLYANICFRHHETS-GDLATEYLQLMVYV-TKTSIKIPSSHTLM 256
Qy
             201 MTLTNGRLRVPQDGRYYLYSQVYFRYPSPSDSDQSSVSHQLVQCIYKKTSYLNPIQ--LL 258
Db
         257 KGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qy
                259 KGVGTKCWAPDAEYALHSVYQGGLFELRAGDEVFVSVSSPTMVYGEDSSSYFGAFRL 315
Dh
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RESULT 6
Q7T1F2
ID
    Q7T1F2
                PRELIMINARY;
                                       304 AA.
AC
    Q7T1F2;
    01-OCT-2003 (TrEMBLrel. 25, Created)
DT
    01-OCT-2003 (TrEMBLrel. 25, Last sequence update)
DT
    01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DT
    Tumor necrosis factor related apoptosis inducing ligand.
DΕ
    Name=TRAIL;
GN
    Gallus gallus (Chicken).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC
OC
    Gallus.
    NCBI TaxID=9031;
OX
RN
    [1]
    SEQUENCE FROM N.A.
RP
    TISSUE=Spleen;
RC
    Sayed A.A., Horiuchi H.H., Furusawa S., Matsuda H.;
RA
    Submitted (JUL-2003) to the EMBL/GenBank/DDBJ databases.
RL
    EMBL; AB114678; BAC79267.1; -.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR003636; TNF subf.
DR
DR
    Pfam; PF00229; TNF; 1.
    ProDom; PD002012; TNF subf; 1.
DR
     SMART; SM00207; TNF; 1.
DR
     PROSITE; PS00251; TNF 1; 1.
DR
     PROSITE; PS50049; TNF 2; 1.
DR
               304 AA; 34658 MW; DFC128B517747C96 CRC64;
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SQ
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                         27.3%; Pred. No. 4.7e-14;
  Best Local Similarity
           82; Conservative 56; Mismatches 126; Indels
                                                             36;
                                                                 Gaps
  Matches
           38 PHQPPAASRSMFVALLGLGLGQVVCSVALFFYFRAQMDP--NRISEDGTHCI--YRILRL 93
Qу
                 3 PAGGPSPAHTCGAVLVAAVLLQSVCVAVTYIYFTNELKQLWDTYSRSGTACLTGEELGDL 62
Db
           94 HENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLD 153
Qy
                                            ::|: |
                                                       ::
                       :||:| : | | ::|
           63 IQNLD----VVESKDR--VADPCWQVKWHLGKLIKKMMSRI-----LQENMSAINGDRTQ 111
Db
          154 -LAKRSKLEAQP----FAHLTINATDIPSGSHKV-----SLSSWYHD-RGWAKISNM 199
Qy
                                                      : 11
                                                              : |
                             1111 ::
              1::1:
          112 ALSRRDEPPQGPTLRIAAHLTGSSKRSSASPHNYLSYRGIGHKIHSWESSRRGHSFLYNV 171
Db
          200 TFSNGKLIVNQDGFYYLYANICFRHHET---SG--DLATEYLQLMVYVTKTSIKIPSSH 253
Qy
                 ||:|:| | |||:|:|: || |
                                           || :
                                                      ||: |: | :
          172 ELWNGELVVPQTGFYYIYSQTYFRFRENEDEDSGLLERIKNPKQLVQYIYKLT-NYPDPI 230
Db
          254 TLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
                   231 LLMKSARTSCWSKKAEYGLYSVYQGGVFQLKREDRIFVSVSNSDIVDMDKEASFFGAFMI 290
Db
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RESULT 7
TN10 HUMAN
     TN10 HUMAN
                    STANDARD;
                                    PRT:
                                           281 AA.
ID
     P50591;
AC
     01-OCT-1996 (Rel. 34, Created)
DT
DT
     01-OCT-1996 (Rel. 34, Last sequence update)
     01-OCT-2004 (Rel. 45, Last annotation update)
DT
     Tumor necrosis factor ligand superfamily member 10 (TNF-related
DE
     apoptosis inducing ligand) (TRAIL protein) (Apo-2 ligand) (Apo-2L).
DΕ
GN
     Name=TNFSF10; Synonyms=TRAIL, APO2L;
     Homo sapiens (Human).
os
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
     Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OC
     NCBI TaxID=9606;
OX
RN
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RP
     MEDLINE=96111955; PubMed=8777713;
RX
     Wiley S.R., Schooley K., Smolak P.J., Din W.S., Huang C.-P.,
RA
     Nicholl J.K., Sutherland G.R., Davis-Smith T., Rauch C., Smith C.A.,
RA
RA
     Goodwin R.G.;
     "Identification and characterization of a new member of the TNF family
RT
RT
     that induces apoptosis.";
RL
     Immunity 3:673-682(1995).
RN
     [2]
RP
     SEQUENCE FROM N.A.
RC
     TISSUE=Placenta;
     MEDLINE=96278649; PubMed=8663110;
RX
     Pitti R.M., Marsters S.A., Ruppert S., Donahue C.J., Moore A.,
RA
RA
     Ashkenazi A.;
     "Induction of apoptosis by Apo-2 ligand, a new member of the tumor
RT
     necrosis factor cytokine family.";
RT
     J. Biol. Chem. 271:12687-12690(1996).
RL
RN
     SEQUENCE FROM N.A.
RP
RC
     TISSUE=Lymph;
     MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RX
     Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA
     Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA
     Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA
     Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA
     Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA
     Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA
     Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA
     Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA
     Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA
     Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA
     Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA
     Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA
     Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA
     Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA
     Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA
     Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA
     Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RA
     "Generation and initial analysis of more than 15,000 full-length human
RT
     and mouse cDNA sequences.";
RT
```

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Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RL
RN
    X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS) OF 114-281.
RP
RX
    MEDLINE=20017054; PubMed=10549288;
    Hymowitz S.G., Christinger H.W., Fuh G., Ultsch M., O'Connell M.,
RA
     Kelley R.F., Ashkenazi A., de Vos A.M.;
RA
     "Triggering cell death: the crystal structure of Apo2L/TRAIL in a
RT
     complex with death receptor 5.";
RT
    Mol. Cell 4:563-571(1999).
RL
RN
     [5]
    X-RAY CRYSTALLOGRAPHY (2.2 ANGSTROMS) OF 119-281.
RP
     PubMed=10542098; DOI=10.1038/14935;
RX
    Mongkolsapaya J., Grimes J.M., Chen N., Xu X.-N., Stuart D.I.,
RA
     Jones E.Y., Screaton G.R.;
RA
     "Structure of the TRAIL-DR5 complex reveals mechanisms conferring
RT
     specificity in apoptotic initiation.";
RT
     Nat. Struct. Biol. 6:1048-1053(1999).
RL
RN
     X-RAY CRYSTALLOGRAPHY (2.8 ANGSTROMS) OF 114-281.
RP
     MEDLINE=99413670; PubMed=10485660;
RX
     Cha S.-S., Kim M.S., Choi Y.H., Sung B.J., Shin N.K., Shin H.C.,
RA
     Sung Y.C., Oh B.-H.;
RA
     "2.8 A resolution crystal structure of human TRAIL, a cytokine with
RT
     selective antitumor activity.";
RT
     Immunity 11:253-261(1999).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF10A/TRAILR1,
CC
         TNFRSF10B/TRAILR2, TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and
CC
         possibly also to TNFRSF11B/OPG. Induces apoptosis. Its activity
CC
         may be modulated by binding to the decoy receptors
CC
         TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and TNFRSF11B/OPG that cannot
CC
CC
         induce apoptosis.
     -!- COFACTOR: Binds 1 zinc ion and one anionic solvent molecule per
CC
CC
         trimer.
CC
     -!- SUBUNIT: Homotrimer.
     -!- SUBCELLULAR LOCATION: Type II membrane protein (Potential).
CC
     -!- TISSUE SPECIFICITY: Widespread; most predominant in spleen, lung
CC
         and prostate:
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
CC
     This SWISS-PROT entry is copyright. It is produced through a collaboration
CC
     between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC
     the European Bioinformatics Institute. There are no restrictions on its
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     use by non-profit institutions as long as its content is in no way
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     modified and this statement is not removed. Usage by and for commercial
CC
     entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC
     or send an email to license@isb-sib.ch).
CC
     ______
CC
     EMBL; U37518; AAC50332.1; -.
DR
     EMBL; U57059; AAB01233.1; -.
DR
     EMBL; BC032722; AAH32722.1; -.
DR
     PDB; 1D0G; X-ray; A/B/D=114-281.
DR
     PDB; 1D2Q; X-ray; A=114-281.
DR
     PDB; 1D4V; X-ray; B=119-281.
DR
     PDB; 1DG6; X-ray; A=91-281.
DR
     PDB; 1DU3; X-ray; D/E/F/J/K/L=114-281.
DR
     Genew; HGNC:11925; TNFSF10.
DR
     MIM; 603598; -.
DR
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GO; GO:0005887; C:integral to plasma membrane; TAS.
DR
     GO; GO:0005625; C:soluble fraction; TAS.
DR
     GO; GO:0005102; F:receptor binding; TAS.
DR
     GO; GO:0007267; P:cell-cell signaling; TAS.
DR
     GO; GO:0006917; P:induction of apoptosis; TAS.
DR
     GO; GO:0043123; P:positive regulation of I-kappaB kinase/NF-k. . .; IEP.
DR
     GO; GO:0007165; P:signal transduction; TAS.
DR
     InterPro; IPR006052; TNF_family.
DR
     InterPro; IPR008983; TNF_like.
DR
     InterPro; IPR003636; TNF subf.
DR
     Pfam; PF00229; TNF; 1.
DR
     ProDom; PD002012; TNF subf; 1.
DR
     SMART; SM00207; TNF; \overline{1}.
DR
     PROSITE; PS00251; TNF 1; 1.
DR
     PROSITE; PS50049; TNF 2; 1.
DR
     3D-structure; Apoptosis; Cytokine; Metal-binding; Signal-anchor;
KW
     Transmembrane; Zinc.
KW
                                  Cytoplasmic (Potential).
                         17
     DOMAIN
                  1
FT
                                  Signal-anchor for type II membrane
                  18
                         38
     TRANSMEM
FT
                                  protein (Potential).
FΤ
                                  Extracellular (Potential).
                  39
                        281
FT
     DOMAIN
                        230
                                  Zinc.
FT
     METAL
                 230
                 123
                        127
FT
     STRAND
FT
                 149
                        150
     STRAND
                 163
                        165
FT
     STRAND
     STRAND
                 167
                        170
FT
     TURN
                 171
                        172
FΤ
     STRAND
                 173
                        176
FT
                 180
                        193
FT
     STRAND
FT
     TURN
                 198
                        199
FT
     STRAND
                 205
                        213
                 220
                        228
FΤ
     STRAND
                 233
                        234
FT
     TURN
                        250
                 237
FT
     STRAND
                        253
FT
     TURN
                 252
                 255
                        260
FT
     STRAND
                 263
                        265
FT
     HELIX
                        267
                 266
FT
     STRAND
                 270
                        272
FT
     TURN
                 274
                        279
FT
     STRAND
                                    DDAAAF78DAAB2F6D CRC64;
                281 AA; 32509 MW;
     SEQUENCE
                          14.9%; Score 251.5; DB 1; Length 281;
  Query Match
                          24.1%; Pred. No. 5.9e-13;
  Best Local Similarity
                                                                45; Gaps
                                                                            10;
            71; Conservative 61; Mismatches 117; Indels
  Matches
           42 PAASRSMFVALLGLGLGQVVCSVALFFYFRAQMD--PNRISEDGTHCIYRILRLHENADF 99
Qy
              1: :: ::: | | :| :| :| :: |: | |
           10 PSLGQTCVLIVIFTVLLQSLCVAVTYVYFTNELKQMQDKYSKSGIACF-----LKED--- 61
Db
          100 QDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSK 159
Qy
                                           :1::1 :1 ::
               1: : 1 : : 1 ::1
           62 -DSYWDPNDEESMNSPCWQVKW------QLRQLVRKMILRTSEETI----STVQEKQ 107
 Db
          160 LEAQPF----AHLT----INATDIPSGSHKVSL---SSWYHDR-GWAKISNM 199
 Qу
                                    11:1
          108 QNISPLVRERGPQRVAAHITGTRGRSNTLSSPNSKNEKALGRKINSWESSRSGHSFLSNL 167
 Db
```

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200 TFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSHTLMKGG 259
Qу
               168 HLRNGELVIHEKGFYYIYSQTYFRFQEEIKENTKNDKQMVQYIYKYT-SYPDPILLMKSA 226
Db
        260 STKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qy
                227 RNSCWSKDAEYGLYSIYQGGIFELKENDRIFVSVTNEHLIDMDHEASFFGAFLV 280
Db
RESULT 8
CAG33176
                                     281 AA.
    CAG33176
               PRELIMINARY;
                              PRT;
ID
    CAG33176;
AC
    01-JUN-2004 (TrEMBLrel. 27, Created)
DT
    01-JUN-2004 (TrEMBLrel. 27, Last sequence update)
DT
    01-JUN-2004 (TrEMBLrel. 27, Last annotation update)
DT
    TNFSF10 protein.
DE
    TNFSF10.
GN
    Homo sapiens (Human).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OC
OX
    NCBI_TaxID=9606;
RN
    [1]
    SEQUENCE FROM N.A.
RP
    Ebert L., Schick M., Neubert P., Schatten R., Henze S., Korn B.;
RA
    "Cloning of human full open reading frames in Gateway(TM) system entry
RT
RT
    vector (pDONR201).";
    Submitted (JUN-2004) to the EMBL/GenBank/DDBJ databases.
RL
    EMBL; CR456895; CAG33176.1; -.
DR
    SEQUENCE 281 AA; 32509 MW; DDAAAF78DAAB2F6D CRC64;
SQ
                       14.9%; Score 251.5; DB 2; Length 281;
  Query Match
  Best Local Similarity 24.1%; Pred. No. 5.9e-13;
          71; Conservative 61; Mismatches 117; Indels
                                                                   10;
                                                        45; Gaps
          42 PAASRSMEVALLGLGLGQVVCSVALFFYFRAQMD--PNRISEDGTHCIYRILRLHENADF 99
Qу
            ]: :: ::: | | | : | : | : | : | : | |
          10 PSLGQTCVLIVIFTVLLQSLCVAVTYVYFTNELKQMQDKYSKSGIACF-----LKED--- 61
Db
         100 QDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSK 159
Qу
             62 -DSYWDPNDEESMNSPCWQVKW------QLRQLVRKMILRTSEETI----STVQEKQ 107
Db
         160 LEAQPF-----AHLT----INATDIPSGSHKVSL----SSWYHDR-GWAKISNM 199
Qy
                          108 QNISPLVRERGPQRVAAHITGTRGRSNTLSSPNSKNEKALGRKINSWESSRSGHSFLSNL 167
Db
         200 TFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVTKTSIKIPSSHTLMKGG 259
Qу
               168 HLRNGELVIHEKGFYYIYSQTYFRFQEEIKENTKNDKQMVQYIYKYT-SYPDPILLMKSA 226
Db
         260 STKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
                || ::|: ||| || || |:|: : | : |:| |:| | :|::|||| |
         227 RNSCWSKDAEYGLYSIYQGGIFELKENDRIFVSVTNEHLIDMDHEASFFGAFLV 280
Db
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RESULT 9
Q6DHG9
ID
     Q6DHG9
                 PRELIMINARY;
                                   PRT;
                                          299 AA.
AC
     Q6DHG9;
     01-OCT-2004 (TrEMBLrel. 28, Created)
DΤ
     01-OCT-2004 (TrEMBLrel. 28, Last sequence update)
DT
DT
     01-OCT-2004 (TrEMBLrel. 28, Last annotation update)
DE
     Hypothetical protein.
     Brachydanio rerio (Zebrafish) (Danio rerio).
OS
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
     Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC
     Cyprinidae; Danio.
OC
     NCBI TaxID=7955;
OX
RN
     [1]
     SEQUENCE FROM N.A.
RP
     TISSUE=Whole;
RC
     MEDLINE=22388257; PubMed=12477932;
RX
     Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA
     Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA
     Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA
     Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA
     Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA
     Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA
     Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA
     Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA
     Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA
     Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA
     Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA
     Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA
     Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA
     Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA
     Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M., Butterfield Y.S.,
RA
     Krzywinski M.I., Skalska U., Smailus D.E., Schnerch A., Schein J.E.,
RA
     Jones S.J., Marra M.A.;
RA
     "Generation and initial analysis of more than 15,000 full-length human
RT
     and mouse cDNA sequences.";
RT
     Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RL
RN
     [2]
     SEQUENCE FROM N.A.
RP
RC
     TISSUE=Whole;
RA
     Strausberg R.;
     Submitted (JUL-2004) to the EMBL/GenBank/DDBJ databases.
RL
     EMBL; BC076005; AAH76005.1; -.
DR
     Hypothetical protein.
KW
                         33526 MW; BA776793D2F11ED5 CRC64;
                299 AA;
SO
     SEQUENCE
                                                        Length 299;
                           14.8%; Score 249.5; DB 2;
  Query Match
                           28.1%; Pred. No. 9.5e-13;
  Best Local Similarity
            85; Conservative 49; Mismatches 126;
                                                                 43; Gaps
                                                        Indels
  Matches
           44 ASRSM-FVALLGLG--LGQVVCSVALFFYFRAQMDPNR--ISEDGTHCIYRI-LRLHENA 97
Qy
                                               : :
                                                              1: 1
                                                       |:
                             | | | :
                                        1 11
            6 SSHTMQYIGLLLLAAILLQTIAVAVTFIYFSNVLSTMKETFSKSSVSCLMRANLRTIKGQ 65
Db
           98 DFQDTTLESQDTKLIPDSCRRIKQ-----AFQGAVQKELQHIVGSQHIRAEKAMVDG 149
Qу
                             | | :: |
                                              :
                                                     111:
                                                           |\cdot|: |\cdot|
                      1:1
           66 ELNGA--EGKD-----DPCWQVTQQLHFLIEKSMSSRYQKEITSAVKDEVSRVLPSLVIQ 118
Db
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150 SWLDLAKRSKLEAQPFAHLTINATDIPSG--SHKV---SLSSWYHDRGWAKISNMTFSNG 204
Qу
                119 DQED-SSRPKIAAHVTGSYTPESEKDGAGLPNRKVYGQKIQSWESEKGLAFLQNVELSDG 177
Db
         205 KLIVNQDGFYYLYANICFRH---HETSGDLATEY-----LQLMVYVTKTSIKIP 250
Qу
             : || :| ::|
Db
         178 ELVVPOAGLYYIYSQTYFRHTLIEEDESAREDEYGSMGESVRGKPMLQYVYKKVSSYQVP 237
         251 SSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYFGA 310
QУ
                                       | | |:| ||: : : ||| | :| |: :::|||
                      | || :||: |||
         238 I--LLMKNARTTCWSRDSEYGLYSIYQAGLFQLGSGDRVFVTVSNVSTIDMDEKSSFFGA 295
Db
         311 FKV 313
QУ
             1 1
         296 FLV 298
Db
RESULT 10
TN10 MOUSE
    TN10 MOUSE
                  STANDARD;
                                 PRT;
                                       291 AA.
ID
    P50592;
AC
    01-OCT-1996 (Rel. 34, Created)
DT
    01-OCT-1996 (Rel. 34, Last sequence update)
DT
    05-JUL-2004 (Rel. 44, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 10 (TNF-related
DΕ
    apoptosis inducing ligand) (TRAIL protein).
DE
    Name=Tnfsf10; Synonyms=Trail;
GN
os
    Mus musculus (Mouse).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OC
OX
    NCBI TaxID=10090;
RN
     [1]
    SEQUENCE FROM N.A.
RP
    MEDLINE=96111955; PubMed=8777713;
RX
    Wiley S.R., Schooley K., Smolak P.J., Din W.S., Huang C.-P.,
RA
    Nicholl J.K., Sutherland G.R., Davis-Smith T., Rauch C., Smith C.A.,
RA
     Goodwin R.G.;
RA
     "Identification and characterization of a new member of the TNF family
RT
     that induces apoptosis.";
RT
     Immunity 3:673-682(1995).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF10A/TRAILR1,
CC
        TNFRSF10B/TRAILR2, TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and
CC
        possibly also to TNFRSF11B/OPG. Induces apoptosis. Its activity
CC
        may be modulated by binding to the decoy receptors
CC
        TNFRSF10C/TRAILR3, TNFRSF10D/TRAILR4 and TNFRSF11B/OPG that cannot
CC
        induce apoptosis.
CC
     -!- SUBUNIT: Homotrimer (By similarity).
CC
     -!- SUBCELLULAR LOCATION: Type II membrane protein (Potential).
CC
     -!- TISSUE SPECIFICITY: Widespread.
CC
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     _____
CC
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CC
     between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC
     the European Bioinformatics Institute. There are no restrictions on its
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     use by non-profit institutions as long as its content is in no way
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     modified and this statement is not removed. Usage by and for commercial
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CC
    or send an email to license@isb-sib.ch).
CC
CC
DR
    EMBL; U37522; AAC52345.1; -.
DR
    HSSP; P50591; 1D2Q.
DR
    MGD; MGI:107414; Tnfsf10.
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    ProDom; PD002012; TNF subf; 1.
DR
DR
    SMART; SM00207; TNF; 1.
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
DR
    Apoptosis; Cytokine; Signal-anchor; Transmembrane.
KW
                          Cytoplasmic (Potential).
FT
               1 17
                             Signal-anchor for type II membrane
               18
                      38
FT
    TRANSMEM
                             protein (Potential).
\mathbf{FT}
    DOMAIN 39 291
CARBOHYD 52 52
                             Extracellular (Potential).
بالما
                            N-linked (GlcNAc. . .) (Potential).
FT
    SEQUENCE 291 AA; 33477 MW; 3FEACAB9F0D7D802 CRC64;
SO
                      14.7%; Score 248; DB 1; Length 291;
  Query Match
  Best Local Similarity 25.4%; Pred. No. 1.2e-12;
          79; Conservative 52; Mismatches 100; Indels 80; Gaps
         46 RSMFVALLGLG-LGQVVCSVALFFYFRAQMD--PNRISEDGTHCIYRILRLHENADFQDT 102
Qy
            17 RMMVICIVLLQVLLQAVSVAVTYMYFTNEMKQLQDNYSKIGLACFSK----TDEDFWDS 71
Db
         103 TLESQDTKLIPDSCRRIK------QAFQ------GAVQKEL 131
Qy
            | | ::: | ::| : | |
         72 T----DGEILNRPCLQVKRQLYQLIEEVTLRTFQDTISTVPEKQLSTPPLPRGGRPQKVA 127
Db
         132 OHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIPSGSHKVSLSSWYHDR 191
Qу
             || | |: |:: |:| | |
                                                         : [] [
         128 AHITGITR-RSNSALI-----PISKDGKTLGQ------KIESWESSR 162
Db
         192 -GWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYL-----QLMVYV 242
Qу
             163 KGHSFLNHVLFRNGELVIEQEGLYYIYSQTYFRFQEAED--ASKMVSKDKVRTKQLVQYI 220
Db
         243 TKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPD 302
Qу
             221 YKYT-SYPDPIVLMKSARNSCWSRDAEYGLYSIYQGGLFELKKNDRIFVSVTNEHLMDLD 279
Db
         303 QDATYFGAFKV 313
Qу
            1:1::1111:
         280 OEASFFGAFLI 290
Db
RESULT 11
Q9DDZ5
                                     214 AA.
               PRELIMINARY;
ID
    Q9DDZ5
AC
    Q9DDZ5;
     01-MAR-2001 (TrEMBLrel. 16, Created)
DT
     01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
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01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DT
DΕ
    TRAIL-like protein.
    Name=tnfsf101;
GN
os
    Brachydanio rerio (Zebrafish) (Danio rerio).
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC
OC
    Cyprinidae; Danio.
OX
    NCBI_TaxID=7955;
RN
    [1]
    SEQUENCE FROM N.A.
RP
    Bobe J., Goetz F.W.;
RA
    "Molecular cloning and expression of a TNF receptor and two TNF
RT
    ligands in the fish ovary.";
RT
    Comp. Biochem. Physiol. B, Comp. Biochem. 129:475-481(2001).
RL
    EMBL; AF250041; AAG47640.1; -.
DR
DR
    HSSP; P50591; 1D2Q.
    ZFIN; ZDB-GENE-010801-1; tnfsf101.
DR
    GO; GO:0016020; C:membrane; IEA.
DR
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
    GO; GO:0006955; P:immune response; IEA.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
DR
    Pfam; PF00229; TNF; 1.
DR
    ProDom; PD002012; TNF subf; 1.
    SMART; SM00207; TNF; 1.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
              214 AA; 24093 MW; 98C002474FF691AA CRC64;
SO
    SEQUENCE
                        14.3%; Score 240.5; DB 2; Length 214;
  Query Match
                       28.6%; Pred. No. 3.5e-12;
  Best Local Similarity
          61; Conservative 50; Mismatches 83; Indels 19; Gaps
 Matches
         118 RIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAK-RSKLEAQPFAHLTINATDIP 176
Qу
                         :: : : |
           2 KLAEGIKAYISKVTDSIISKQTLHAARTQTHSYNTTGSKFMTTVMQRPSAHLTLSSASDN 61
Db
         177 S-----GSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICF 222
Qy
                           62 SRPQSDMHQPQFDLHQSCRHPVHTWANKSFGAHLYNMTLTNGRLRVPQDGRYYLYSQVYF 121
Db
         223 RHHETS-GDLATEYLQLMVYV-TKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGF 280
Qy
             122 RYPSPSDSDQSSVSHQLVQCIYKKTSYLNPIQ--LLKGVGTKCWAPDAEYALHSVYQGGL 179
Db
         281 FKLRSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qy
             180 FELRAGDEVFVSVSSPTMVYGEDSSSYFGAFRL 212
Db -
RESULT 12
090WT9
                                       287 AA.
                PRELIMINARY;
                                PRT;
ID
     Q90WT9
AC
     Q90WT9;
     01-DEC-2001 (TrEMBLrel. 19, Created)
DT
     01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT
     01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
ידת
```

```
TNF-related apoptosis inducing ligand-like protein.
    Gallus gallus (Chicken).
OS
    Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
    Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC
OC
OX
    NCBI TaxID=9031;
RN
    [1]
RP
    SEQUENCE FROM N.A.
RA
    Bridgham J.T., Johnson A.L.;
    Submitted (OCT-2001) to the EMBL/GenBank/DDBJ databases.
RL
DR
    EMBL; AY057941; AAL23702.1; -.
DR
    HSSP; P50591; 1D2Q.
DR
    GO; GO:0016020; C:membrane; IEA.
    GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
    GO; GO:0006955; P:immune response; IEA.
DR
DR
    InterPro; IPR006053; TNF abc.
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DŔ
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
    PRINTS; PR01234; TNECROSISFCT.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; \overline{1}.
DR
DR
    PROSITE; PS50049; TNF 2; 1.
              287 AA; 32092 MW; DB06E1C95087B108 CRC64;
SO
                        12.8%; Score 216.5; DB 2; Length 287;
 Query Match
  Best Local Similarity 24.7%; Pred. No. 5.7e-10;
                                                            25; Gaps
                                                                        6;
          61; Conservative 57; Mismatches 104; Indels
          80 SEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQH 139
Qy
             51 SSEELRCLQLINQQQEGSNLEEL-----ISNQSCLKLANTIKAYVATVTENVISRSV 102
Db
         140 I-RAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATDIP----SGSHKVSLSSW 187
Qу
             : |:|: :| :| :| :| || :
                                                           | \cdot | ::: |
         103 VNEAQKSYFNISEGQVA--TKTLGKPSAHLIFRPQNPAQDGSSRRFGNLSQSCRHAITRW 160
Db
         188 YHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATEYLQLMVYVT-KTS 246
Qу
                  11:::111
         161 EDSTIHSHLQNITYRDGRLRVNQAGKYYVYSQIYFRYSRDGAGARVSVPQLVQCINWKTS 220
Db
         247 IKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDAT 306
Qу
                   221 YSQPI--LLLKGVGTKCWAPEAEYGLHALYQGGLFELKAGDELFVSVSSLAIDYSDAAAS 278
Db
         307 YFGAFKV 313
Qу
             11111::
         279 YFGAFRL 285
Db
RESULT 13
Q8K3G0
                                       287 AA.
ID
     Q8K3G0
                PRELIMINARY;
AC
     Q8K3G0;
     01-OCT-2002 (TrEMBLrel. 22, Created)
DT
     01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
\mathbf{DT}
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01-MAR-2004 (TrEMBLrel. 26, Last annotation update)
DT
         TNF-related apoptosis inducing ligand.
DE
OS
         Rattus norvegicus (Rat).
         Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
         Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OC
OX
         NCBI TaxID=10116;
RN
         [1]
RP
         SEQUENCE FROM N.A.
         STRAIN=DA;
RC
         Mueller A.M., Giegerich G.;
RA
         Submitted (MAY-2002) to the EMBL/GenBank/DDBJ databases.
RL
         EMBL; AY115578; AAM49797.1; -.
DR
         HSSP; P50591; 1D2Q.
DR
         GO; GO:0016020; C:membrane; IEA.
DR
         GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
         GO; GO:0006955; P:immune response; IEA.
DR
         InterPro; IPR006052; TNF family.
DR
         InterPro; IPR008983; TNF like.
DR
         InterPro; IPR003636; TNF subf.
DR
         Pfam; PF00229; TNF; 1.
DR
         ProDom; PD002012; TNF subf; 1.
DR
         SMART; SM00207; TNF; \overline{1}.
DR
         PROSITE; PS00251; TNF_1; UNKNOWN 1.
DR
         PROSITE; PS50049; TNF 2; 1.
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SQ
                                                 12.8%; Score 215.5; DB 2; Length 287;
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                    73; Conservative 59; Mismatches 113; Indels
                                                                                                                         57; Gaps
                                                                                                                                                14;
    Matches
                     42 PAASRSMFVALLGLGLGQVV---CSVAL-FFYFRAQMD--PNRISEDGTHCIYRILRLHE 95
Qу
                                      ::::|||:::||::::||:::||:::||::||:::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::||::
                     10 PSFSQHFTMTVICIVLLQVLLQALTVAVTYMYFNNEVKQLQDNYSKIGLACFSK----E 64
Db
                     96 NADFQDTTLESQDTKLIPDSCRRIKQAFQGAVQKELQHIVGSQHIRA-EKAMVDGSWLDL 154
Qy
                                               65 DGDFWDST----DEGILNRPCLQVK------RQLYQLIEEVTLRTFEKT-----IST 106
Db
                   155 AKRSKLEAQPF-----AHLT----INATDIPSGSHKVSL----SSWYHD-RGWA 194
Qу
                                  107 VPEKQLSTPPLPRGRRPQRVAAHITGITRRSNLALIPISKDGKTLGQKIETWESSRRGHS 166
Db
                   195 KISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLAT-----EYLQLMVYVTKTSIK 248
Qy
                                          ||:|:::::| ||:|::: :| |
                                                                                                                     1:: 1: 1:
                   167 FLNHVHLRNGELVIQEEGLYYIYSQTYYRFKEAKEASKTVSKDGGRIKQMVQYIYKYT-S 225
Db
                   249 IPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEEISIEVSNPSLLDPDQDATYF 308
Qy
                                                 226 YPDPILLMKSARNSCWSREAEYGLYSIYQGGLFELKENDRIFVSVTNEHLMDLDHEASFF 285
Db
                   309 GA 310
Qy
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                   286 GA 287
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ID
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AC
     28-FEB-2003 (Rel. 41, Created)
     28-FEB-2003 (Rel. 41, Last sequence update)
DT
     05-JUL-2004 (Rel. 44, Last annotation update)
DT
    Tumor necrosis factor ligand superfamily member 6 (FAS antigen
DΕ
DΕ
     ligand).
    Name=TNFSF6; Synonyms=FASL;
GN
     Sus scrofa (Pig).
OS
     Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC
     Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OC
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OX
RN
     [1]
     SEOUENCE FROM N.A.
RP
     MEDLINE=21322533; PubMed=11429161; DOI=10.1089/107999001300177493;
RX
     Muneta Y., Shimoji Y., Inumaru S., Mori Y.;
RA
     "Molecular cloning, characterization, and expression of porcine Fas
     ligand (CD95 ligand).";
RT
     J. Interferon Cytokine Res. 21:305-312(2001).
RL
RN
     SEQUENCE FROM N.A.
RP
     STRAIN=Guanxi bama miniature pig;
RC
     Zhu N., Young Y.;
RA.
     "Molecular cloning and characterization of porcine Fas ligand cDNA.";
RT
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RL
RN
RP
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RC
     TISSUE=Lymphoid;
     Tsuyuki S., Kono M., Bloom E.T.;
RA
     "Cloning and potential utility of porcine Fas ligand: overexpression
RT
     in porcine cells protects them from attack by human cytolytic cells.";
RT
     Submitted (JUL-2001) to the EMBL/GenBank/DDBJ databases.
RL
RN
RP
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     STRAIN=Landrace x Large Yorkshire white; TISSUE=Thymocytes;
RC
     MEDLINE=21653191; PubMed=11792426;
RX
     Motegi-Ishiyama Y., Nakajima Y., Hoka S., Takagaki Y.;
RA
     "Porcine Fas-ligand gene: genomic sequence analysis and comparison
RT
RT
     with human gene.";
     Mol. Immunol. 38:581-586(2002).
RL
     -!- FUNCTION: Cytokine that binds to TNFRSF6/FAS, a receptor that
CC
         transduces the apoptotic signal into cells. May be involved in
CC
         cytotoxic T cell mediated apoptosis and in T cell development.
CC
         TNFRSF6/FAS-mediated apoptosis may have a role in the induction of
CC
         peripheral tolerance, in the antigen-stimulated suicide of mature
CC
         T cells, or both. Binding to the decoy receptor TNFRSF6B/DcR3
CC
         modulates its effects (By similarity).
CC
     -!- SUBUNIT: Homotrimer (Probable).
CC
     -!- SUBCELLULAR LOCATION: Type II membrane protein and secreted (By
CC
CC
         similarity).
CC
     -!- INDUCTION: By IL-18.
     -!- PTM: The soluble form derives from the membrane form by
CC
CC
         proteolytic processing (By similarity).
     -!- SIMILARITY: Belongs to the tumor necrosis factor family.
CC
     CC
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CC
     between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC
```

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    or send an email to license@isb-sib.ch).
CC
    _______
CC
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DR
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DR
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DR
    InterPro; IPR006053; TNF abc.
DR
    InterPro; IPR006052; TNF family.
DR
    InterPro; IPR008983; TNF like.
DR
    InterPro; IPR003636; TNF subf.
DR
    Pfam; PF00229; TNF; 1.
DR
    PRINTS; PR01681; FASLIGAND.
DR
    PRINTS; PR01234; TNECROSISFCT.
DR
    ProDom; PD002012; TNF subf; 1.
DR
    SMART; SM00207; TNF; 1.
DR
    PROSITE; PS00251; TNF 1; 1.
DR
    PROSITE; PS50049; TNF 2; 1.
DR
    Apoptosis; Cytokine; Glycoprotein; Signal-anchor; Transmembrane.
KW
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FT
    CHAIN
                  1
                       282
                                 member 6, membrane form.
FT
                                 Tumor necrosis factor ligand superfamily
FT
     CHAIN
                131
                       282
                                 member 6, soluble form (By similarity).
\mathbf{FT}
                                 Cytoplasmic (Potential).
     DOMAIN
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                        82
FT
                                 Signal-anchor for type II membrane
FT
     TRANSMEM
                 83
                       103
                                 protein (Potential).
FT
                104
                       282
                                 Extracellular (Potential).
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     DOMAIN
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                        70
                                 Pro-rich.
\mathbf{FT}
     DOMAIN
                        56
                                 Poly-Pro.
                 45
FT
     DOMAIN
                                 Cleavage (By similarity).
                130
                       131
FT
     SITE
                203
                       234
                                 Potential.
FT
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                                 N-linked (GlcNAc. . .) (Potential).
                185
                       185
FT
     CARBOHYD
                                 N-linked (GlcNAc. . .) (Potential).
                       251
                251
FT
     CARBOHYD
                                 N-linked (GlcNAc. . .) (Potential).
FT
     CARBOHYD
                261
                       261
                                 F \rightarrow L (in Ref. 4).
                 5
                        5
FT
     CONFLICT
                                 T \rightarrow P (in Ref. 2).
                        57
                 57
FT
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Qу
              H + L
                                      11:
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Db
           52 LLGLGLGQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKL 111
Qу
                      :| | | : | : |
              1: | | | | |
           95 LVGLGLG-----MFQLFHLQKE----- 124
Db
          112 IPDSCRRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLT-- 169
Qу
                             : |: :| :: :||
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125 -----ELRKVAHLTGK 153
Db
         170 INATDIPSGSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSG 229
Qy
                                 - 1
         154 PNSRSIP-----LEWEDTYGIALVSGVKYMKGSLVINDTGLYFVYSKVYFRGQYCN- 204
Db
         230 DLATEYLQLMVYVTKTSIKIPSSHTLMKGGSTKY-----WSGNSEFHFYSINVGGFFKL 283
Qу
                 : 1
                      1: :1
         205 ---NQPLSHKVY-TRNS-RYPQDLVLMEGKMMNYCTTGQMWARSS-----YLGAVFNL 252
Db
         284 RSGEEISIEVSNPSLLDPDQDATYFGAFKV 313
Qу
              | : : : || ||:: :: |:|| :|:
         253 TSADHLYVNVSELSLVNFEESKTFFGLYKL 282
Db
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     01-JUN-2003 (TrEMBLrel. 24, Created)
DT
     01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT
     01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
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DE
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     Felis silvestris catus (Cat).
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OC
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OC
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RP
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     Mizuno T., Endo Y., Momoi Y., Goto Y., Nishimura Y., Tsubota K.,
RA
     Mikami T., Ohno K., Watari T., Tsujimoto H., Hasegawa A.;
RA
     "Molecular cloning of feline Fas antigen and Fas ligand cDNAs.";
RT
     Vet. Immunol. Immunopathol. 65:161-172(1998).
RL
     EMBL; AB009280; BAC76426.1; -.
     HSSP; P01374; 1TNR.
DR
     GO; GO:0005576; C:extracellular; IEA.
DR
     GO; GO:0016020; C:membrane; IEA.
DR
     GO; GO:0005164; F:tumor necrosis factor receptor binding; IEA.
DR
     GO; GO:0006915; P:apoptosis; IEA.
DR
     GO; GO:0006955; P:immune response; IEA.
DR
     GO; GO:0007165; P:signal transduction; IEA.
DR
     InterPro; IPR008064; Fas ligand.
DR
     InterPro; IPR006053; TNF abc.
DR
     InterPro; IPR006052; TNF family.
DR
     InterPro; IPR008983; TNF like.
DR
     InterPro; IPR003636; TNF subf.
DR
     Pfam; PF00229; TNF; 1.
DR
     PRINTS; PR01681; FASLIGAND.
DR
     PRINTS; PR01234; TNECROSISFCT.
DR
     ProDom; PD002012; TNF subf; 1.
     SMART; SM00207; TNF; 1.
DR
     PROSITE; PS00251; TNF_1; 1.
DR
     PROSITE; PS50049; TNF 2; 1.
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               280 AA; 31361 MW; 6AA7E2DE1F1A6B5C CRC64;
SO
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Qу		20	GGPGAPHEGPLHAPPPPAPHQPPAASRSMFVALLGLG 56	5
Db	1	38	GRPGQRRPPPPPPTLPPPPPPPPPPPPPPPPLPLPLPLKTRRDHNTGLCLLVMFFMVLVALVGLG 97	7
Qу	•		LGQVVCSVALFFYFRAQMDPNRISEDGTHCIYRILRLHENADFQDTTLESQDTKLIPDSC 11	۱6
Db	,	98	LGKELAELRESTSQKH 12	21
Qy	,	117	RRIKQAFQGAVQKELQHIVGSQHIRAEKAMVDGSWLDLAKRSKLEAQPFAHLTINATD 17	74
Db	)	122	VASSLEKQIGQLNPPSEKRELRKVAHLTGKPNSRS 15	6
Qy	,	175	<pre>IPSGSHKVSLSSWYHDRGWAKISNMTFSNGKLIVNQDGFYYLYANICFRHHETSGDLATE 23   </pre>	34
Db	•	157	IPLEWEDTYGIALVSGVKYKKGGLVINDTGMYFVYSKVNFRGQSCNNQ 20	)4
QΣ	7	235	YLQLMVYVTKTSIKIPSSHTLMKGGSTKYWSGNSEFHFYSINVGGFFKLRSGEE 28	38
Dk	>	205	PLNHKVYMRNSKYPQDLVLMEGKMMNYCTTGQMWARSSYLGAVFNLTSADH 25	55
Qζ	7	289	ISIEVSNPSLLDPDQDATYFGAFKV 313 : :         : :   :   :   :	
DŁ	)	256	LYVNVSELSLVSFEESKTFFGLYKL 280	

Search completed: November 8, 2004, 18:32:13 Job time: 194 secs